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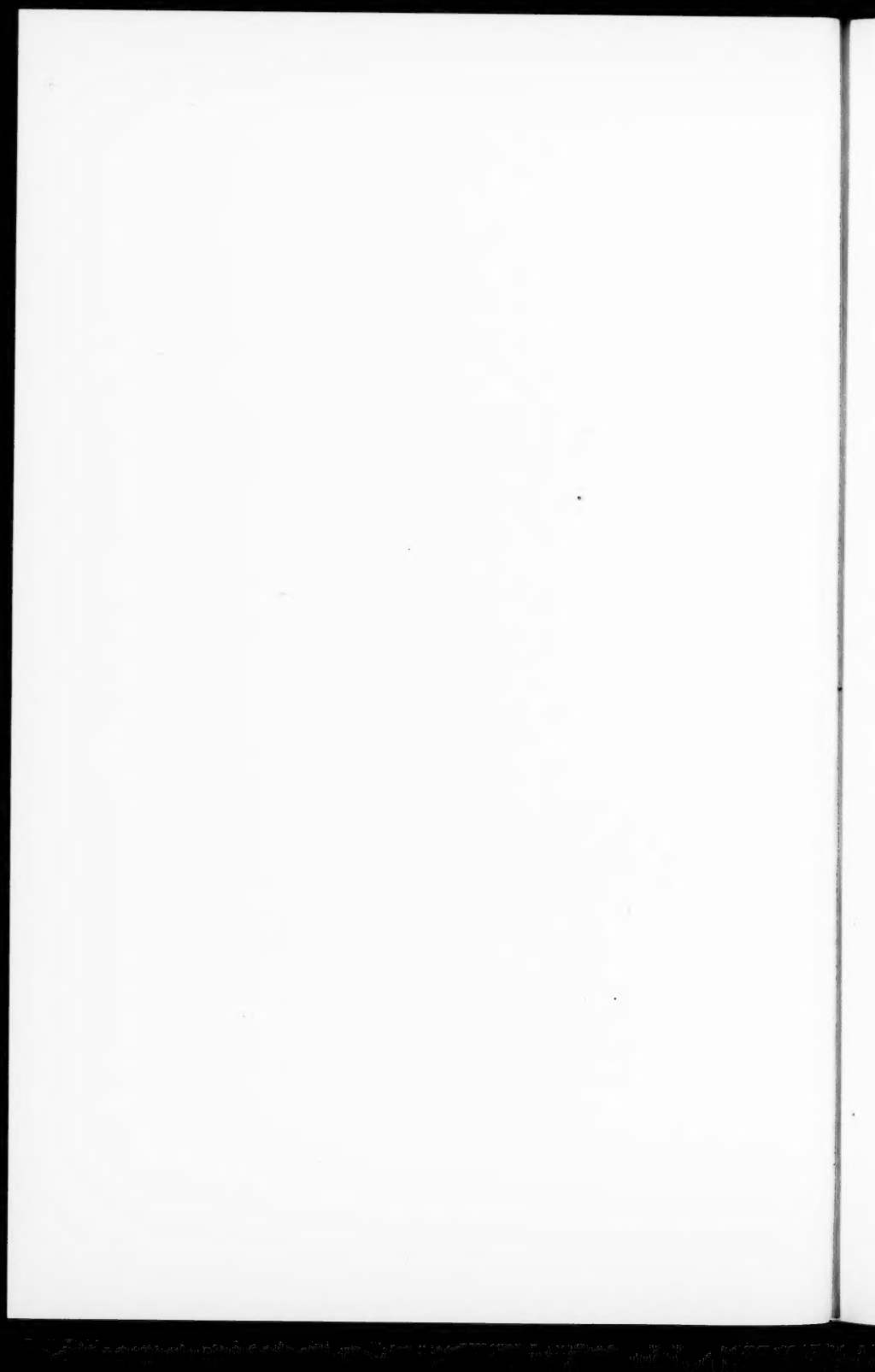
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# THE MEDICAL CLINICS OF NORTH AMERICA

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CLINIC OF DR. DAVID RIESMAN

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## A LECTURE ON PNEUMONIA WITH SPECIAL REFERENCE TO DIAGNOSIS AND TREATMENT.

ALTHOUGH it is unnecessary before an audience such as this to dwell on elementary principles, I shall take the liberty of stating a few important facts that should be borne in mind in any study of pneumonia.

1. The cause of lobar pneumonia is in the vast majority of cases the pneumococcus.

2. The pneumococcus, although macroscopically unitary, is biologically subdivisible into a number of varieties, which are apparently genuine species and breed true. The following table shows the proportionate occurrence of the four established types in 454 cases<sup>1</sup>:

Pneumococcus type.	Incidence.	Per cent.
I.....	151	33.3
II.....	133	29.3
II (atypical) <sup>2</sup> .....	19	4.2
III.....	59	13.0
IV.....	92	20.3

<sup>1</sup> Avery, Chickering, Cole, and Dochez: Monograph 7, Rockefeller Institute for Medical Research, October 16, 1917, p. 18.

<sup>2</sup> The incidence of atypical Type II pneumococci has been determined only during the last two years.

3. The pneumococcus of pneumonia is rarely a normal inhabitant of the mouth. It is, however, found in the entourage of pneumonia patients and in those convalescent from pneumonia. This fact is important in the epidemiology of the disease, and suggests the probability that the disease is conveyed by carriers.

The subjoined table, giving the experience of the Rockefeller Institute, bears out very clearly the fact that those in contact with pneumonia patients harbor to a considerable degree the pathogenic organisms in the mouth, while those not exposed do so very rarely:

Pneumococcus.	Contacts.		Non-contacts.	
	Number examined.	Percentage positive.	Number examined.	Percentage positive.
Type I.....	160	13	297	0.3
Type II.....	149	12	297	0

4. Pneumonia is a transmissible disease. Theoretically every case harks back to another, but practically such a relationship is not always, indeed, not very often, traceable. The same thing is, however, often true of diphtheria, typhoid fever, tuberculosis, etc. The contagiousness of pneumonia must be admitted. It will be interesting to watch the results of the compulsory quarantine recently inaugurated in Pittsburgh.

The possibility of transmission in less direct ways than contact should be considered. It might be a wise rule to require that all cases of illness among persons living on premises where food, including milk, is handled or where drinking-water is bottled should be reported to the health authorities if the illness has lasted longer than three days.

5. Pneumonia is often preceded by a slight cold, which seems to make the individual more susceptible. Increased virulence of the organisms is also a possible factor. Bad climatic conditions, excessive aerial dust contamination, and severe mental strain act as predisposing causes.

6. The immunity produced by one attack of pneumonia is not permanent. Susceptibility returns, hence recurrence of attacks in the same patient. It may be that subsequent attacks

are brought about by other types of pneumococci in persons whose general resistance has been lowered by the first attack.

7. Pneumonia occurs epidemically, although it is rarely absent in sporadic form in any large community. The mortality of different epidemics varies, but, on the whole, there seems to be a gradual though moderate decline in the death-rate. It is very difficult to obtain satisfactory statistics regarding pneumonia. The deaths are reported, but only a small proportion of the cases, hence we know the total mortality but not the total morbidity, nor the relation the former bears to the latter. In New York City, as I am informed by Dr. Louis I. Harris, Director of the Bureau of Preventable Diseases, not more than 30 per cent. of the cases of pneumonia are reported. Sometimes it happens in our large cities that the deaths from pneumonia exceed the total number of cases reported.

In order to know more about the epidemiology of pneumonia it should be made a reportable disease, even if no quarantine is instituted. The physician in charge and the Boards of Health should endeavor to trace the source whenever possible. I believe the time will come when quarantine will be the rule in our large cities.

Although in its origin probably bronchiogenic or aërogenic, pneumonia soon becomes a general infection with localization chiefly in the lungs and pleura. The pneumococcus may, however, localize in other parts, in the arteries and veins, producing thrombosis, in the joints, the peritoneum, the meninges, the middle ear, the tonsils.

The crisis of pneumonia is one of the most mysterious phenomena in nature. If understood it would open a vast field of unexplored territory. Whether it is due to autolysis of the organisms or to rupture of equilibrium between ferment and anti-ferment in the blood, as maintained by Jobling and Petersen, is unknown.

The general symptoms of pneumonia are in part due to the pneumotoxin, in part to protein substances contained in the exudate in the lungs.

Many years ago I called attention to the fact that we must reckon in the pathogenesis of infectious diseases with products of cellular growth and degeneration in addition to bacterial toxins. Quantitatively considered the cells in the exudate in the lung are equal in number to the bacteria, since both for practical purposes are infinite. Just as bacteria in their growth and decay may produce toxic substances, so the cells in the pulmonary exudate in their cycle from birth to death may give rise to metabolic and other products that play a part as yet unknown in the clinical picture of pneumonia. The same principles apply to typhoid fever, to miliary tuberculosis, and to other proliferative diseases.

While the pneumococcus is by all odds the chief cause of pneumonia, a word should be said about other causes, such as the streptococcus, the influenza organism whatever it may be, and other bacteria, as well as the *Monilia pulmonalis*.<sup>1</sup>

#### DIAGNOSIS

In the majority of cases the diagnosis is easy; a sudden onset of illness, pain in the side, cough and fever, rusty sputum, and leukocytosis spell pneumonia. In young children and senile persons the diagnosis is often difficult. It is also difficult when pneumonia develops as a complication during the course of some other malady. I shall point out some of the errors and some of the ways of avoiding them.

**Pneumonia Without Signs in the Chest.**—Quite often in children, but by no means infrequently in adults, one meets cases that start out like pneumonia, with chill and high fever, but with little or no cough, and without definite signs in the chest. After ruling out tonsillitis and the acute eruptive fevers search should be made for evidence of pneumonia. The most satisfactory explanation of these cases is that the disease begins as a central pneumonia spreading afterward to the periphery. By careful examination it is usually possible to find some change in the physical signs in the lungs, especially if one looks in two particular spots, near the angle of the scapula and in the axilla. In one of these areas a change will be found in the percussion

<sup>1</sup> Johns, New Orleans Medical and Surgical Journal, July 8, 1924.

note over a spot perhaps not larger than a silver dollar. The note is a little shortened rather than dull. On auscultation the breath sounds are muffled or suppressed, on coughing a few fine râles are usually heard; the voice will have a twangy quality. If in addition to these signs and symptoms the patient has an expiratory grunt, the diagnosis of pneumonia is justified. A high leukocyte count is a valuable corroborative sign, but is not always present.

**Pneumonia With Abdominal Symptoms.**—The most confusing cases are those in which the pneumonia begins with abdominal symptoms. I have seen pneumonia simulate appendicitis<sup>1</sup> as well as gall-stone colic; in one case an acute pleurisy was mistaken for acute pancreatitis. In all these instances the pain was located in the region of the organ that was supposed to be diseased. We are beginning through the work of Sherrington and Head and Mackenzie to understand these referred pains a little better. However, they will frequently trip the unwary.

It is, I think, a good rule not to diagnosticate acute appendicitis or other acute abdominal disease until one has by thorough exploration of the chest excluded pneumonia and pleurisy. The leukocyte count is not of decisive value because both appendicitis and pneumonia cause a marked increase in the number of white cells; but we should always be made cautious and reflective if the leukocytes in a suspected case of abdominal disease are above 20,000.

**Postoperative Pneumonia.**—Regarding the diagnosis of postoperative pneumonia, one must bear in mind that it may not present typical signs and symptoms. There may be no cough and no pain of particular severity, only a little fever and increase in respiration rate. As the lesion is rarely in front, one is apt to miss it if one does not make it a practice to examine the lower lobes posteriorly and the axillary regions. Even if the patient cannot be lifted or turned, it is usually possible to slip the stethoscope under the back.

<sup>1</sup> Adams and Berger (Jour. Amer. Med. Assoc., 79, 1809, November 25, 1922) state that of 145 cases sent into the Boston City Hospital as appendicitis, 25 proved to be cases of pneumonia.

The nature of postoperative pneumonia is a subject much discussed. The evidence is increasing that the primary condition is collapse or atelectasis of a part of the lung, the collapsed area afterward becoming consolidated.

Pneumonia follows more often upon abdominal than upon pelvic operations.

I might allude for a moment to *massive collapse of the lungs*, a rare postoperative complication. The physical signs are dullness or dull tympany on percussion and displacement of the heart toward the side affected. As a rule the breath sounds over the dull area become bronchial after a few days, indicating that lobar pneumonia has supervened. Recognition of these cases is important, as is pointed out by Lund and Ritvo,<sup>1</sup> on account of the relatively good prognosis under conservative treatment and of the serious consequences which may come if the patient is tapped or the pleura explored under a mistaken diagnosis.

Postoperative pneumonia is in some measure a preventable disease. No operation, unless it be of an emergency character, should be undertaken in any patient who has the slightest catarrhal inflammation of the respiratory tract. Better protection of the patient against chilling and drafts during his transfer to and from the operating room and in the etherizing room is very desirable. A third point of importance is guarding the patient against the contagion of colds after the operation through the visits of solicitous friends or nurses and doctors suffering from colds.

I believe if these three principles are followed postoperative pneumonia will be much less common than it is today.

**Pneumonia Simulating Other Diseases.**—I have already mentioned the fact that pneumonia may simulate abdominal diseases. It may also resemble typhoid fever and meningitis. It very frequently resembles pleurisy.

**Other Diseases Resembling Pneumonia.**—It is but natural that certain other diseases of the chest should be mistaken for pneumonia. This is particularly true of *tuberculosis*. The so-

<sup>1</sup> C. C. Lund and M. Ritvo, *Boston Medical and Surgical Journal*, June 26, 1924.



called phthisis florida may in the beginning be indistinguishable from acute lobar pneumonia. As a general rule, however, the differentiation which is most important from the standpoint of the patient and for the doctor's reputation can be made by attention to the following points:

1. Leukocytosis is usually but not invariably absent.
2. The physical signs on careful investigation show a slight aberration from the usual.
3. There is a history of some failure of health prior to the acute onset, perhaps an earlier pleurisy, loss in weight, failure of appetite.
4. Acute tuberculous pneumonia nearly always affects the upper lobe. If the lower lobe is affected it will usually be along its upper margin.

*Pulmonary Infarct.*—This may closely resemble acute lobar pneumonia. It can be diagnosed from it by the fact that the patient often sits up in infarct, which he does not do in pneumonia. The temperature is usually low, and definite evidence of cardiac disease is present.

*Pulmonary congestion*, such as is found in typhoid fever and in decompensating heart lesions after severe attacks of angina pectoris, etc., can be differentiated by the following features:

1. Congestion is usually bilateral.
2. If unilateral it is reversible, that is, it will be found to change with changing posture of the patient, so that only the lower side, whichever it may be, shows the râles.
3. There is no true bronchial breathing.
4. There is an adequate underlying cause.

A curious error may arise during the course of *acute pericarditis*. With the development of an effusion of considerable size one often can detect over the left lung posteriorly percutory and auscultatory signs of consolidation due to compression of the lung by the effusion. I might call it *pericarditic pseudopneumonia*. Without direct experience one will surely consider it true pneumonia and nothing else. Its diagnosis hinges on the remembered fact of its existence.

*Pyelitis.*—In rare cases pyelitis may simulate pneumonia as

is illustrated by the following case: Mrs. F., a pregnant woman, suddenly was seized with chill, fever, and pain in the lower chest and flank. Her physician naturally suspected lobar pneumonia. When I came to examine her I found nothing whatever in the lungs, but detected a sharp point of tenderness in the right loin and obtained a history of slight urinary disturbance. I ventured a diagnosis of acute pyelitis, which was borne out by examination of the urine and by the subsequent course of the case. Pyelitis is a frequent mischief maker for the diagnostician; it must be kept in mind whenever a protracted fever has no obvious explanation.

#### PNEUMONIA IN CHILDREN<sup>1</sup>

I shall epitomize the salient points of this phase of the subject:

1. Lobar pneumonia is more common in infants and children than the text-books teach. Even the pneumonia of measles is often typically lobar.

2. The physical signs of primary lobar pneumonia are at times late in appearing. The combination of high fever with leukocytosis is suggestive.

3. The signs may be apical or basal; sometimes they appear first in the axilla.

4. An expiratory grunt is a very suggestive symptom.

5. Convulsions, delirium, and meningeal symptoms are common in the pneumonia of young children.

6. Abdominal symptoms, pain, tenderness, and vomiting are often present and mask the pneumonia.

7. Lesné's scalene sign<sup>2</sup> may be of value, but I have had no personal experience with it. This sign consists in immobility of the subclavicular region in apical pneumonia due to contraction of the scaleni inserted in the first and second ribs. It may be discerned by palpating the lateral muscles of the neck between the sternocleidomastoid and the trapezius. The firm,

<sup>1</sup> Riesman, Jour. Amer. Med. Assoc., April 19, 1924, vol. 82, p. 1256.

<sup>2</sup> Lesné, Bull. soc. de pédiat. de Paris, 22, 64. February-March, 1924; Int. Survey Med., July, 1924.

tense condition of the muscles occurs only on the side affected.

8. Empyema is a frequent termination, and manifests itself by continuing fever, pallor, sweating, etc.

9. Primary lobar pneumonia in children is a very benign disease; even if empyema develops, the prognosis is good, conditioned of course on proper treatment.

#### THE HEART IN PNEUMONIA

Endocarditis is surprisingly rare in pneumonia, but just as rare as is endocarditis, so common is myocarditis or at least myocardial change. Cardiac weakening together with the mechanical obstacle presented by the consolidated lung and perhaps the high position of the diaphragm through tympany, have a tendency to lead to right-sided overloading of the heart.

Abnormalities of rhythm are not common, but I have seen auricular flutter and also fibrillation. We should bear in mind, of course, that digitalis in large doses may lead to arrhythmia.

The blood-pressure is an important guide, but I do not believe that the so-called Gibson rule is without exception. According to Gibson, when the blood-pressure expressed in millimeters falls below the pulse-rate so that the two cross, the prognosis is bad. As I have just indicated, this rule has exceptions.

#### TREATMENT

The treatment of pneumonia is, after all, the most important subject pertaining to the disease. In its present form it is far from satisfactory, and has not reached a stage commensurate with our progress in some other common infectious diseases.

**Preventive Treatment.**—The preventive treatment of the disease does not compare in efficiency with that attained in typhoid fever or diphtheria and which I hope may soon be reached in scarlet fever. The vaccines employed in the preventive treatment have not given very satisfactory results, although it seems probable that when pneumonia is prevailing as a virulent epidemic, the use of mixed vaccines may be fairly effective. Disinfection of the sputum is undoubtedly indicated as one of the preventive measures of pneumonia. With regard

to quarantine, I am not prepared to express a definite opinion, as I should like to await the results of the Pittsburgh experiment in this direction.<sup>1</sup> However, since the pneumococci appear very quickly in the mouth of persons about the pneumonia patient, the physician should institute his own quarantine.

The **curative treatment** of pneumonia divides itself into: (a) specific treatment, (b) general treatment, (c) treatment of complications.

(a) Specific treatment. This is of five types:

I. Use of serums from immunized animals.

II. Serum from otherwise healthy patients convalescing from pneumonia.

III. Serum or blood from birds, chiefly chickens.

IV. Use of extracts or antibodies made from the pneumococci themselves.

V. Chemotherapy.

I. Regarding the treatment with serum from immunized animals it seems to be fairly well established that it is possible to obtain a potent serum which is both antitoxic and bactericidal against pneumonia due to Type I pneumococcus, but that serums against other types of pneumococci are practically without avail.

Through the use of Type I serum the mortality has not been reduced sufficiently to give such serum the rank of an ideal specific.

In the administration of antipneumococcic serums the following points should be observed:

1. They must be given as early as possible.

2. They must be given intravenously.

3. They must be given in large amounts.

4. There is some danger from anaphalaxis which can be guarded against by preliminary desensitization. It is best combated by injections of adrenalin.

5. Serum sickness very frequently follows and is a most depressing sequel. I remember a man, a great lover of horses and

<sup>1</sup> I have just heard that quarantine for pneumonia has been in vogue in Los Angeles for some time.

a horseback rider, in whom the treatment proved worse than the disease. It is true he recovered from a severe attack of pneumonia, but he was troubled with joint swellings and some myocardial weakness for a long time.

II. The use of serum from convalescent patients has been abandoned.

III. The use of chicken blood and chicken blood-serum as advocated by Keyes has not become popular, although Berger and Montgomery<sup>1</sup> report favorable results in a small series of cases. Of 38 patients treated with the serum, 5 died, and of 23 without the serum, 8 died. But such statistics are entirely too small when it comes to a disease like pneumonia to be of any value. On the whole, chicken blood-serum is a questionable agent.

IV. The antibodies have been prepared in various ways, the aim being to remove as much of the toxic proteins as possible. Those most employed and most studied have been the Huntoon antibody solutions, which in the hands of a few persons have given better results than have been obtained by any other form of treatment. There are some drawbacks to their use. They must be given intravenously; they must be given in large amounts and must be repeated; they produce a severe reaction, particularly a violent chill. My own experience with the Huntoon bodies is limited, but I cannot say that the results obtained have been in any sense brilliant.

Cecil, with a much larger experience, is more enthusiastic about them. He tried the subcutaneous or intramuscular route in the hope that it would obviate the violent reaction. Such injections, however, were far less efficacious and have now been abandoned.

A few months ago Dr. Felton, of Harvard, announced that he had prepared a much more refined antibody solution than that of Huntoon, but I have not been able to ascertain what results have followed the use of the Felton preparation.

#### V. Chemotherapy.

1. *Quinin*.—The treatment of pneumonia by quinin is old.

<sup>1</sup> Jour. Missouri State Med. Assoc., 21, 137, May, 1924.

It was recommended by Sir Dominick Corrigan in the first third of the nineteenth century. While quinin has a distinct inhibitory influence upon the pneumococcus *in vitro*, I do not believe that it ranks as a specific in the treatment of human infection. But just as arsenic by itself in the ordinary preparations is valueless against syphilis, but in certain organic combinations, as in arsphenamin, becomes a specific remedy, so quinin in organic combination may develop into a valuable, perhaps a curative agent.

You are familiar with optochin (ethylhydrocuprein) which is powerfully bactericidal both in the test-tube and in experimental pneumococcus infection in animals. In the human subject, however, the therapeutic dose and the toxic dose are so close together as to make the drug unsafe.

2. *Mercurochrome*.—This new and very promising agent has been found useful in blood infection with septic organisms. It has given good results in pneumonia due to the streptococcus, but so far it has not been tested sufficiently in pneumococcus pneumonia to warrant any definite conclusion.

A word about the *cold-air treatment*—if employed routinely in all cases it does harm. It should be used only in those patients that are vigorous. *Diathermy* has been recommended by several recent writers as a satisfactory method of treating lobar pneumonia.<sup>1</sup> Stewart<sup>2</sup> in 40 cases not treated by diathermy had a mortality of 42.9 per cent.; in 12 cases treated by diathermy the mortality was 20 per cent. I have had no personal experience, but the number of cases so far treated is so small that statistics are of no value.

**General Treatment.**—As far as I know there is, aside from the uncertain specific measures I have mentioned, no better method of lessening the toxemia than by maintaining a free flow of urine and keeping the bowels open. The best diuretic is an abundance of water. One should try to obtain from 50 to 70 ounces of urine a day.

There are certain general rules of importance in the treatment of pneumonia. They may be stated as follows:

<sup>1</sup> Lacey, Jour. Radiology, June, 1924.

<sup>2</sup> Stewart, R. I., Med. Jour., October, 1923.

1. The less handling the better.
2. No sponging except in unusual cases.
3. No company.
4. Ice-cap to the head and alkalinization of the patient.

For the purpose of alkalinizing the patient I have found the following mixture very satisfactory:

Sp. ammon. aromat.....	10
Liq. ammon. acetat.....	40
Liq. potass. citrat. enough to make	150

A tablespoonful in water every three or four hours.

One should always bear in mind the possibility of retention of urine in pneumonia patients, and should make it a rule at every visit to percuss the bladder region and to inquire into the urine output.

The diet should consist of cooked cereals, fruit juices, milk or buttermilk, poached or soft-boiled egg, junket, plain custard, wine jelly, water-ice.

If there is nausea, which is rare, ginger ale or charged water may be used.

*Myocardial failure*, the most frequent route into the unknown for the pneumonia patient, is best combated by a proper anticipatory and prophylactic treatment. This consists in the use of digitalis from the beginning in any patient who is decidedly sick. It matters little how the digitalis is administered, whether in massive doses or in small interrupted doses.

Robert Levy<sup>1</sup> has shown that in those cases in which digitalis is not used dilatation of the heart is much more likely to set in.

The preparation of the drug used is also not important, provided an efficient one, of which there are a number obtainable, is employed.

Myocardial failure in its severest type manifests itself usually near the time of the expected crisis. It may become acute and reach alarming proportions, for the successful combating of which the physician needs a definite, well-planned, routine

<sup>1</sup> Archives Int. Med., 32, 359, September 15, 1923.

treatment. I may epitomize this as follows: If a patient is developing pulmonary edema, one of the most common manifestations, the following measures should be employed: Atropin in large doses, gr. 1/75, repeated in two hours if necessary; digitalis hypodermically; caffein-sodium benzoate and camphorated oil. Dry cupping may also prove useful.

If there is marked cyanosis with or without pulmonary edema, venesection is indicated and perhaps the use of oxygen.

Tympany is a frequent and distressing symptom in pneumonia patients having marked toxemia. The treatment consists in the external application of turpentine stupes, the use of the rectal tube, asafetida enemas, and pituitrin hypodermically.

Insomnia is a common symptom and is best controlled by bromids or morphin sulphate.

Cough, if distressing or if it keeps the patient awake, must be combated either with codein or with morphin.

What about the use of alcohol? It is not necessary in the average case, but seems to be of great value in septic pneumonias and in the pneumonia of alcoholics.

A word about the treatment of pneumonia in children. Without impropriety I may call myself a progressive in medicine, and yet I feel that in the pneumonia of children an old-fashioned procedure, somewhat condemned by those who consider themselves ultramodern, is eminently useful, and that is the flaxseed poultice.

#### COMPLICATIONS

Among the complications to which I should like to call attention is, first, hemoptysis. I have seen a few patients who bled so profusely that without a careful examination and study the diagnosis would have been tuberculosis. The cause of such profuse hemorrhage is usually intense congestion of the lungs. The possibility that the patients are bleeders must be borne in mind.

**Jaundice** is quite common, and, as a general rule, is not a serious symptom. It may, however, become an element of great gravity if it reaches a marked degree. In such cases the symptoms of general toxemia—muttering delirium, tympany, hypotension—are pronounced. I shall not at this time discuss the causes of jaundice in pneumonia.



**Thrombophlebitis.**—This is a fairly common sequel of pneumonia, which usually ends in perfect recovery, although a tendency to swelling of the leg may persist for a long time.

Among other complications may be mentioned otitis media, arthritis, and parotitis.

**Meningitis**, if genuine and not merely a toxic irritation, the so-called meningism, is usually a fatal complication, although of late some recoveries from pneumococcic meningitis have been reported.

**Delirium tremens** is now quite rare, and because it is rare one is apt not to be thinking of it, especially not in private practice.

**Acute dilatation of the stomach** is a rare complication capable of presenting great diagnostic difficulties. The symptoms are vomiting, abdominal pain, distention of the abdomen, visible gastric peristalsis, obstinate constipation, more rarely diarrhea, and collapse. Under prompt treatment, which consists of gastric lavage through a stomach-tube, recovery usually ensues.

**Diabetes.**—Strictly speaking the complication here is the pneumonia, not the diabetes. Pneumonia in diabetic patients constitutes one of the gravest of dangers, but I believe that with large doses of insulin it will be possible to save life. In the early days of insulin therapy I lost a case probably because I was afraid to use large doses of insulin.

#### DELAYED RESOLUTION

Using this term in a purely clinical sense to imply a failure to get well in a reasonable time, we find that the causes are manifold:

1. There may be a delay due to failure of proper liquefaction of the exudate through a lack of ferments or through an excess of antiferments.

2. Empyema. This is one of the commonest causes of so-called delayed resolution. It may be interlobar or free, and is to be suspected in every case in which pneumonia lasts beyond the normal time. Pallor, sweating, and irregular fever justify exploratory puncture.

3. Abscess of the lung is more common than is usually believed. It may readily be mistaken for empyema. Careful physical examination aided by the x-ray will usually differentiate between these two allied conditions.

4. Tuberculosis. This must be considered from two points of view:

(a) Tuberculosis may supervene upon a true lobar pneumonia in a patient who has had latent tuberculosis.

(b) As I pointed out before, what appears to be lobar pneumonia may in reality be a tuberculous caseous pneumonia.

5. Pericarditis: This may easily be overlooked. As it usually is purulent, recognition may mean proper surgical treatment and the saving of life.

6. Syphilis, as has been shown by Fitz-Hugh, may be the cause of persistence of physical signs in pneumonia. It is, therefore, a good practice, when delay in resolution is not otherwise explained, to make a Wassermann test.

7. Various other complications of less moment may delay recovery—arthritis, middle ear disease, perhaps hepatitis.

8. Sometimes a peculiar pulmonary edema remains for a long period in the lobe that had been the seat of the pneumonic process. The cause of this, which I would call *residual edema*, is difficult to ascertain.

#### CONVALESCENCE

There is one more point to which I should like to call your attention, namely, convalescence. We are beginning to realize the importance of conserving health; we have always realized the importance of combating disease; we have not realized sufficiently the importance of watching over convalescence. The pneumonia patient, after he is over his acute attack, needs time to recuperate; the older he is, the more time he needs. Whenever possible such a patient should be sent away to a favorable climate for at least two weeks, preferably longer, before resuming work. The investment will abundantly pay for itself in protecting the heart and vessels from premature degeneration.

## CLINIC OF DR. O. H. PERRY PEPPER

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### NON-INFECTIOUS LEUKOCYTOSIS

#### Cases presented:

1. Cerebral hemorrhage with leukocyte count, 16,600.
2. Ruptured ectopic gestation with leukocyte count, 23,800.
3. Paroxysmal tachycardia with leukocyte count, 17,100.

GENTLEMEN: In this hour<sup>1</sup> I plan to discuss with you certain phases of the subject of leukocytosis. At once I sense the reaction of some of you—"Why, that's old stuff, we learned all about that last year," and yet I am going to brave your disapproval. The tools most used most need to be kept sharpened, and there are few diagnostic tools used more frequently and regularly by the physician, surgeon, and specialist than is the leukocyte count. Familiarity breeds carelessness, and the careless daily use of the leukocyte count results in certain misconceptions as to its full significance and limitations.

If, as in certain psychologic tests, I say to you the word "leukocytosis" and ask for your first associated word, I am sure that the majority will give the word "infection." This is correct as far as it goes, but there is a dangerous fallacy in the assumption that all leukocytosis is the result of infection. It is, of course, true that infection is the most frequent cause of leukocytosis, and that in every-day practice it is in the diagnosis of infections that the leukocyte count finds its greatest value. But by no means does a leukocytosis always mean infection, nor does every infection bring about an increase in the leukocyte count. Serious errors in diagnosis may readily be made if one fails to remember these facts.

<sup>1</sup> Outline of a Clinic to a Senior Class in Medicine, University of Pennsylvania.

In the first place, the so-called normal leukocyte count of 7500 is not absolutely constant, and even in the normal individual it is subject to many slight variations during each twenty-four hours.<sup>1</sup> These are known as physiologic variations, and the classical examples of physiologic leukocytoses, as you probably remember, are in the newborn, in the later weeks of pregnancy, during labor, after heavy exercise, during digestion, and after cold baths and certain other conditions which probably should be interpreted in terms of blood flow and blood volume.<sup>2</sup> It is one thing to know that such physiologic increases in leukocyte count occur and to memorize the commoner causes, but it is far harder to apply this knowledge at the bed-side properly to evaluate the leukocyte count made after the epileptic seizure, the uremic convulsion, or the heavy meal. It is true that such leukocytoses are not, as a rule, marked, seldom exceeding 13,000; it is also true that much help will be gained from the differential count. The pitfall, however, is there for the unwary.

In the newborn infant the count may be over 20,000. Bakwin and Morris<sup>3</sup> have shown that this leukocytosis is not dependent on changes in blood concentration, nor is it any higher in babies with dehydration fever than in normals. By the end of the first week of life the count has settled, as a rule, to between 10,000 and 12,000.

In the later weeks of pregnancy an apparently physiologic leukocytosis is sometimes seen, perhaps more frequently in primiparae. During labor the count rises abruptly, often to 20,000 and sometimes to 30,000; in uncomplicated cases this drops to normal within a few days.<sup>4</sup> It is not known whether the leukocytosis of labor is due to the exertion, the loss of blood, or to some still unrecognized factor. It is difficult to believe that it is due entirely to the exertion, as the leukocytosis which follows other forms of exertion seldom if ever exceeds 15,000. During menstruation a slight increase is often observed.

<sup>1</sup> Glaser and Buschmann, *Med. Klin.*, 1923, 19, 1144.

<sup>2</sup> Bacon, Novy, and Eppler, *Arch. Int. Med.*, 1922, 30, 229.

<sup>3</sup> *American Journal Diseases of Children*, 1923, 26, 23.

<sup>4</sup> Stengel, *New York Medical Journal*, 1903, 63, 56.

Digestive leukocytosis is inconstant and of no great magnitude; interest in it, however, has been revived by the recent claim of Widal<sup>1</sup> and his associates, that the changes in the leukocyte count after a protein meal can be used as a test of hepatic function. It is claimed that if the so-called "proteopexic" function of the liver is impaired a protein meal will be followed by a reduction in the white cell count just as if a foreign protein were gaining entrance to the blood. This so-called "hemoclastic list" is not proving very satisfactory in actual practice.

Leukocytosis may result from disturbed blood flow or from altered blood volume, and this may in the final analysis be the mechanism by which many of the physiologic leukocytoses are produced. Such changes in the leukocyte count as are brought about by changes in blood flow or volume are, of course, analogous to the changes in the red cell count, as, for example, secondary polycythemia, brought about by similar factors. The leukocyte count will be increased by slowing of the bloodstream whether due to local stasis or to failure of the general circulation. Even position, vasomotor influences, and changes in temperature are sufficient to alter slightly the white cell count.<sup>2</sup> These changes are all of them very slight and clinically of no great importance.

Severe acute circulatory failure may at times, however, be accompanied by an apparently non-infectious leukocytosis of such a degree as to make the recognition of its true origin a matter of the utmost diagnostic importance. Anyone who has seen a case of coronary thrombosis in which there were some upper abdominal symptoms will realize how an associated leukocytosis might help to lead one to a mistaken diagnosis. In Wearn's<sup>3</sup> excellent article on coronary thrombosis some amazingly high counts are recorded. Even more amazing perhaps is the leukocytosis recorded in paroxysmal tachycardia; from a normal level during the intermission between attacks the count may rise to over 20,000 in the paroxysm of rapid heart action and in-

<sup>1</sup> Presse Méd., 1920, 28, 893.

<sup>2</sup> Tinel, La Médecine, 1923, 4, 463.

<sup>3</sup> Amer. Jour. Med. Sci., 1923, 165, 250.

efficient circulation. Here again is opportunity for diagnostic error. The onset of the leukocytosis is so sudden and the return to normal so prompt after the cessation of the paroxysm that one cannot help but believe that the leukocytosis is the result of a mere redistribution of cells. The mechanism at work may be in part circulatory stasis, but it is also possible that during such periods of circulatory inefficiency there occurs such a contraction of the mouth of the arterioles leading to large capillary beds, that while plasma continues to enter the area, cells are excluded. This would obviously result in an increase in numbers in the rest of the blood-stream. Recent observations by Richards in the course of his kidney investigations suggest that this might well occur. Changes in blood volume would, of course, effect the blood-count, but, unfortunately, the methods for the satisfactory clinical determination of the blood volume are still lacking, and our knowledge along this line waits on a more readily applicable method. Changes in the leukocyte count such as those reported by Bostrom<sup>1</sup> after the introduction into the body of acids and alkalies will probably be found to be dependent on some such factor.

A great variety of organic and inorganic substances are known to produce leukocytosis, moderate or slight in most instances it is true, but still worthy of mention. There is probably no uniformity in the way in which the increased count is brought about by these different substances; some may act on the blood volume or blood flow, while others may be true stimulators of leukocyte proliferation. The literature is filled with reports concerning the action of one individual substance or another, but there is little evidence as to the mechanism by which the leukocytosis is produced.

Included in the list of such substances are the following: extracts from highly cellular organs, adrenin, nuclein, collargol, turpentine, camphor, antipyrin, phenacetin, digitalis preparations, pyrocin, pyrogallol, benzol derivatives, arsphenamin, and long-continued chloroform narcosis. Some of these are also found in the list of substances which reduce the leukocyte

<sup>1</sup> Amer. Jour. Physiol., 1924, 67, 291.

count, for example, the benzol derivatives. It is probably largely a matter of dosage whether a stimulation perhaps very temporary, or a depressant effect probably more lasting, of the hemopoietic system is obtained.<sup>1</sup> Analogous is the slight temporary leukocyte increase which may follow radiation, while a larger dose lowers the count.

Leukocytosis occurs in certain disease conditions in which there is apparently no infection present and in which one is led to suspect a more direct chemical course. For example, uremia is often accompanied by a moderate leukocytosis in which infection probably plays no part. Here again the finding of a leukocytosis might direct one's thoughts into faulty lines. Similarly, after operative procedures, even in the absence of any evidence of infection, a very definite, although moderate, leukocytosis may appear probably due to the absorption of the products of tissue breakdown incident to the trauma of the operation. The occurrence of such a leukocytosis after a supposedly clean operation might readily give apprehension of an infectious complication unless its real nature was appreciated. This slight leukocytosis might appear quite considerable if a normal count had been recorded just before the operation.

Another type of non-infectious leukocytosis is that which appears after hemorrhage. It has been known for many years that a very moderate increase of leukocyte count occurs after any severe hemorrhage, but it is only more recently that proper emphasis has been given to the much greater leukocytosis which follows bleeding into the peritoneum, the pleura, the intradural space or a joint cavity. An excellent article on this subject appeared last year by Wright and Livingston.<sup>2</sup> In such instances of bleeding into a serous space the leukocyte count may rise to 20,000 or even 30,000 per cubic millimeter; the peak is reached in about ten hours after the hemorrhage and the leukocytosis persists as a rule for four days. From a practical point of view the leukocytosis following intraperitoneal bleeding is probably the most important.

<sup>1</sup> Emge and Jensen, *Jour. Pharm. and Exp. Therap.*, 1921, 17, 415.

<sup>2</sup> *New York State Journal of Medicine*, 1923, 23, 286.

Hoessli<sup>1</sup> was among the first to draw attention to the leukocytosis which accompanies intraperitoneal bleeding. Levinson<sup>2</sup> has reported a count of 22,000 in a case of ruptured tubal pregnancy, Govaerts, 31,000 from a ruptured spleen. In the 28 observations made on cases of ruptured ectopic gestation Wright and Livingston found the average figure on the first day to be 20,200 white cells per cubic millimeter. It takes but an instant's thought to appreciate how readily such a count in a patient with acute abdominal symptoms might lead the physician or surgeon, unfamiliar with the possibility of posthemorrhagic leukocytosis, to make a mistaken diagnosis of some intra-abdominal infection.

Similarly, the clinical importance of leukocytosis with intradural hemorrhage is obvious. Apparently an immediate high leukocyte count is a constant accompaniment of cranial injury if associated dural hemorrhage is present. Wright and Livingston go so far as to say that the absence of leukocytosis in a case with cranial injury excludes the possibility of fracture of the base of the skull.

In the various forms of posthemorrhagic leukocytosis it appears that the degree of leukocytic increase is not always proportional to the amount of bleeding. The counts which occur following even a moderate intradural hemorrhage are far higher than those which follow a massive external hemorrhage; this suggests that two different mechanisms may be at work in the two different forms. In external hemorrhage it would seem that the actual loss of blood must be the responsible factor, although an element of absorption from the point of bleeding may be present. On the other hand, the higher counts from bleeding into a serous space would seem to be due largely, if not wholly, to the absorption of some substance stimulating the formation of leukocytes. Certainly the leukocytosis in these cases, for example, of intraperitoneal bleeding, is a true leukocytosis in the sense that young immature cells enter the blood. Probably an increased proliferation of leukocytes actually occurs, since immature leukocytic forms, even myelocytes, may appear in the

<sup>1</sup> Mitt. a. d. Grenzgeb. d. M. u. Chir., 1914, 27, 630.

<sup>2</sup> Jour. Amer. Med. Assoc., 1915, 64, 1294.



circulating blood. Similarly, erythropoietic stimulation is suggested by the finding of nucleated red cells during the period of leukocytosis.

It may be proper to suggest that the moderate leukocytosis which occasionally accompanies tuberculous peritonitis or tuberculous meningitis may in causation be analogous to post-hemorrhagic leukocytosis rather than to infectious leukocytosis. Usually, as you know, infection with the tubercle bacillus does not bring about a leukocytosis, but in certain forms of this infection, especially those just mentioned, exceptions to this rule not so infrequently occur. Perhaps the same element of absorption acts in these cases to produce a leukocytosis as it does after hemorrhage into a serous space.

Neoplasms may have a slight leukocytosis associated with them, but it is not known what the causative factor is. Carcinoma and sarcoma apparently act similarly, although there is a wide-spread impression that leukocytosis is more common and higher with sarcoma than with carcinoma. When metastasis to bone with involvement of red marrow occurs, then leukocytosis becomes much more constant and often considerable. Counts of over 40,000 leukocytes per cubic millimeter have been reported. The encroachment on the marrow by the tumor may act by simple direct irritation in the production of this form of leukocytosis.

Finally, moderate leukocytosis is known to occur in terminal or agonal states. Of course, terminal bacterial invasion may be responsible in such cases, or the increase of leukocytes may be simply relative or secondary to some such factor as altered blood volume or blood flow.

In this brief review of the non-infectious causes of leukocytosis little mention has been made of any of the changes in the differential count which may be associated. There is, of course, no question of the truth of the statement that leukocytosis achieves its full usefulness in diagnosis and prognosis only when it is accompanied by a differential count of the leukocytes. This is especially true in the differentiation of infectious from non-infectious leukocytoses such as we are now considering. In a clear-cut case of active infection where one

count has, for example, been 15,000 cells with 85 per cent. of them neutrophils, a later count of 20,000 may need no differential count to reveal its full significance. On the other hand, there are many instances in which a very slight leukocytosis with, however, a markedly increased percentage of neutrophils may be far more indicative than a higher total count with a normal or almost normal differential picture.

Physiologic leukocytosis is often not associated with any change in the differential count, while the reverse is usually the case where infection is the cause of a leukocytosis. It is clear that a differential count should be made in every case with leukocytosis even of a slight degree. Sometimes it will increase the significance of the leukocytosis; at other times it will lessen it, but it will always be worth while. In fact, there are not a few who if limited to but one method would choose the differential count rather than the total count of leukocytes.

Similarly, in various types of leukocytosis young forms of leukocytes appear in the blood to a different degree. In the very slight physiologic leukocytoses there may not only be no change in the differential count, but no increase in young forms may occur. This is usually measured by the so-called "Arneth method," about which Arneth has written an entire large book.<sup>1</sup> In this method the neutrophils, for example, are divided into five classes according to their age as determined from the increasing irregularity of the nucleus: Class I has a single round or more or less indented nucleus, while in Class V the nucleus is composed of five or more distinct lobulations or segments. The percentage of neutrophils falling into these different classes is determined and the relative increase or decrease in young forms or in old forms can be deduced. The figures shown on page 725, taken from Arneth's book, will exemplify the difference between several types of leukocytosis.

The contrast is striking and needs little or no comment. The unchanged formula in the very slight leukocytosis during digestion, the moderate "shift to left," as it is called in the case of postpartum hemorrhage and in the newborn infant, and the

<sup>1</sup> Die qualitative Blutlehre, 1920, Leipzig.

Condition.	Leukocyte count per cubic milli- meter.	Percentage of neutrophils by classes.				
		I.	II.	III.	IV.	V.
Normal adult.....	7,500	4-9	21-47	33-48	9-23	2-4
During digestion.....	9,400	5	30	44	19	2
Postpartum hemorrhage	13,900	24	56	20	0	0
Newborn.....	25,600	20	50	25	3	2
Lobar pneumonia:						
Second day.....	15,400	61	29	9	1	0
Seventh day.....	20,700	56	37	6	1	0
Diphtheria.....	24,900	65	27	7	1	0

marked increase in young forms in the instances of infectious leukocytosis suggest the various mechanisms at work. During digestion there is but a redistribution of cells; following the hemorrhage probably the appearance of some new cells from the bone-marrow, but no great proliferation, while in the infectious leukocytoses an active proliferation is taking place. These figures have been quoted not because this method is widely employed today or is of any great practical value, but because they emphasize the fundamental differences which exist between various forms of leukocytosis.

It is interesting to think back over the growth of our knowledge of the leukocytes, for although it is many years since Hewson first discovered them, Virchow appreciated their importance, and Ehrlich elaborated the tinctorial technic for their subclassification, we are still in the dark on many points. As Bunting,<sup>1</sup> in an excellent review of the subject of the leukocytes, points out, we have as yet no evidence of a purely physiologic function for this group of cells. What little we do know of leukocytic function suggests that it is protective against pathologic dangers. After spending years in refining the classification of leukocytic types based on the staining reactions of nucleus, cytoplasm, and granules, all of which criteria may prove to have no very fundamental significance, we are at last approaching a more desirable classification based on function. We owe much to Sabin's<sup>2</sup> studies on the origin of the blood-cells and on the appearance and behavior of living leukocytes.

<sup>1</sup> *Physiological Reviews*, 1922, 2, 505.

<sup>2</sup> *Ibid.*, 1922, 2, 38.

Three main groups are becoming more and more clearly defined, each with distinct characteristics, each with apparently distinct functions. These are: (1) the granular leukocytes—neutrophilic, eosinophilic, or basophilic; (2) the monocytes, and (3) the lymphocytes.

The group characteristics of the granular leukocytes include rapid ameboid movement, phagocytic power, a proteolytic ferment, and a responsiveness to specific chemical stimuli. The neutrophil acts as a defense against most types of bacterial invasion; the eosinophil is in some manner related to the disposal of foreign protein which has gained entrance to the body. The function of the basophil is not known.

The monocytes (large mononuclear leukocytes, transitional leukocytes, endothelial leukocytes) are as a group characterized by marked activity in the phagocytosis of particulate matter; they are capable of slow movement and they possess oxydase granules perhaps indicative of the presence of proteolytic ferment. These cells rapidly engulf any foreign erythrocytes, colloid material, pigment granules, etc., which may enter the circulation, and they or their close relations are the active phagocytes of the serous spaces. They form an important part of the so-called "reticulo-endothelial system" and have much to do with the destruction of worn-out red blood-cells and with the breakdown of hemoglobin.

The third group, the lymphocytes, reach the circulation largely through the lymph-channels and thoracic duct. Enormous numbers (3,300,000,000 per day in the dog<sup>1</sup>) enter the blood daily in this way, and there is evidence that a large percentage of these cells leave the blood to enter the lumen of the intestine, there to be destroyed and to perform some still unknown function. Apparently the lymphocytes are in some way related to certain forms of immunity and bodily resistance, including that to tuberculosis and possibly to cancer.<sup>2</sup> A hopeful line of cancer investigation has here been opened. As a

<sup>1</sup> Bunting and Huston, *Jour. Exp. Med.*, 1921, 33, 593.

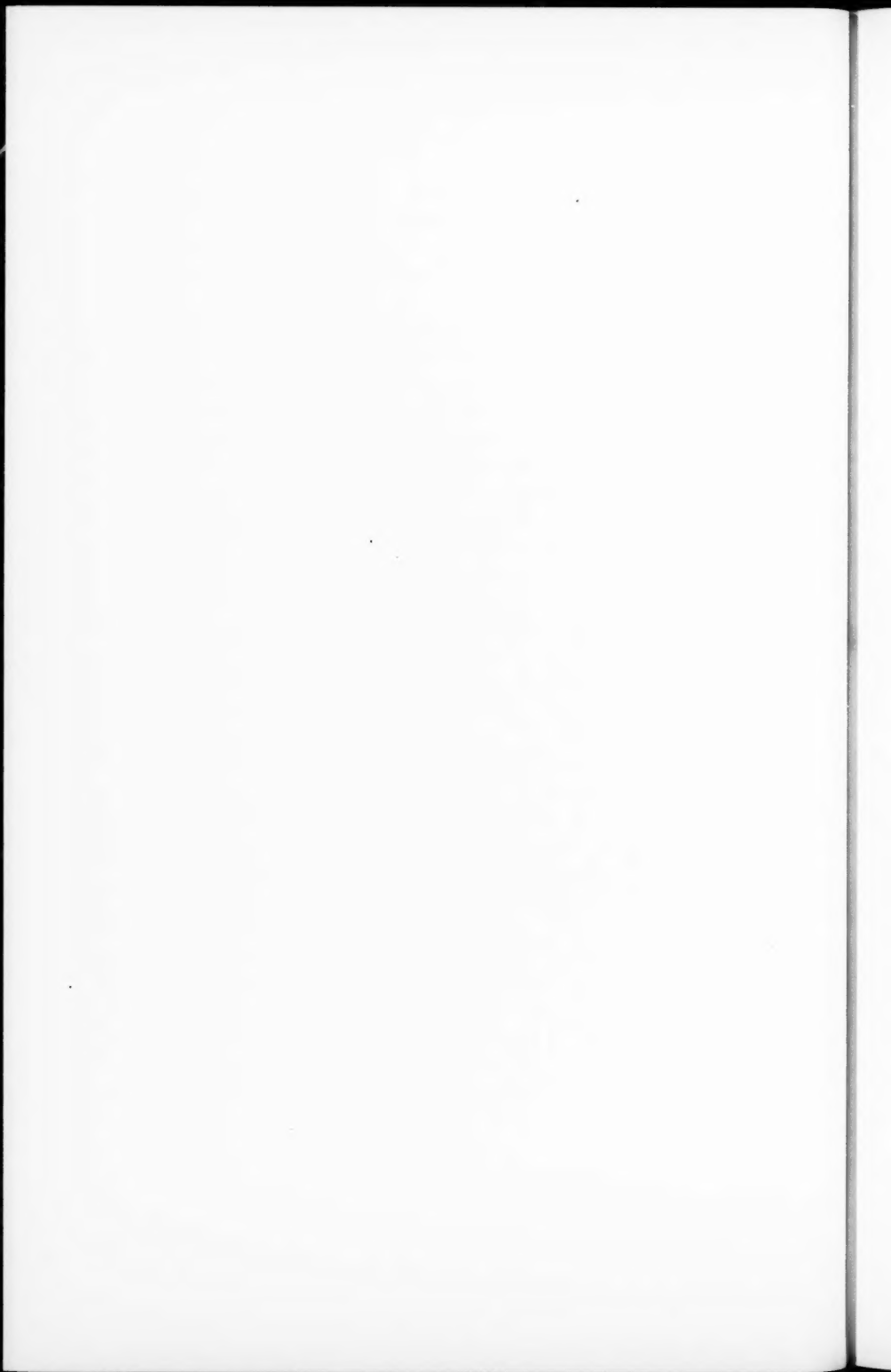
<sup>2</sup> Series of papers by J. B. Murphy and his collaborators in *Jour. Exp. Med.*, starting in 1912.

group these cells are peculiarly sensitive to Roentgen rays and to radium emanations. In contrast to the granular leukocytes and monocytes, the lymphocytes possess no proteolytic or autolytic ferments; they are not phagocytic and have little or no true power of ameboid movement.

With increasing knowledge of the specific function of the various forms of leukocytes our understanding of leukocytosis will be broadened, and it will become more and more possible to appreciate the meaning of an increase of one or another form.

From these brief remarks it must be clear that to think of leukocytosis as always of the same type and always caused by infection is a very inadequate appreciation of the facts. Leukocytosis may result from a wide variety of causes besides infection; it may occur to a slight degree without any change in differential count and without the appearance of any immature or any marked increase in young forms. For the proper analysis of a leukocytosis these various considerations must be kept in mind.

In practical every-day medicine the leukocyte count plays an important part, and we must constantly be on our guard not to be misled by it. In the great majority of cases there is little danger of error, but in the occasional instances, such as those which have been quoted, the danger of serious diagnostic error is very real. The danger is the greater because owing to our familiarity with the leukocyte count we do not stop to think of possible pitfalls. To conclude with the thought expressed at the beginning, it is very important that we should be as fully acquainted as possible with the methods which we routinely employ. That this is not always true of us may be suggested by what has been said about so common a method as the leukocyte count.



## CLINIC OF DR. MARTIN E. REHFUSS

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### SOME OBSERVATIONS ON GASTRIC CARCINOMA

CANCER destroys more than 90,000 people in the United States every year, and more than one-third of these are due to cancer of the stomach. If we realize that there are probably at the present time some 300,000 potential cases of carcinoma and almost 100,000 of these are gastric in type, we can visualize the tremendous importance of this problem. Rockey points out that with a 34,293 yearly mortality from cancer of the stomach, the patient is entitled to something better than a guess and a dyspepsia tablet. Roberts in a recent contribution pointed out that one-third of the cancers arising in men affect the stomach, and one-fifth of these lesions in women are gastric. If 38 out of every 100 people who die of cancer have the gastric form of the disease, it becomes necessary to seriously reflect on the only possible solution of the subject in the present state of our knowledge, namely, early diagnosis. The text-book description gives usually an excellent account of the natural history of the disease, but almost every symptom is a death warrant for the patient. Cachexia, anemia, palpable mass, coffee-ground vomitus, anacidity, each and every one of these is an advanced symptom. The *physician must recognize carcinoma of the stomach in its inception*, and all surgical statistics prove that *if the diagnosis is sufficiently early life can be prolonged and even saved*. In spite of the local implantation of radium and cross-fire x-ray, the knife is the only *cure* for carcinoma of the stomach in the present state of our knowledge.

I propose in this short résumé to discuss some of those points which modern diagnostic methods bring up in the course of a

survey for cancer of the stomach. Apart from history and physical signs there are two methods which are indispensable, namely, the Roentgen study and intubation. Obviously, there is a latent period in the development of the disease in which

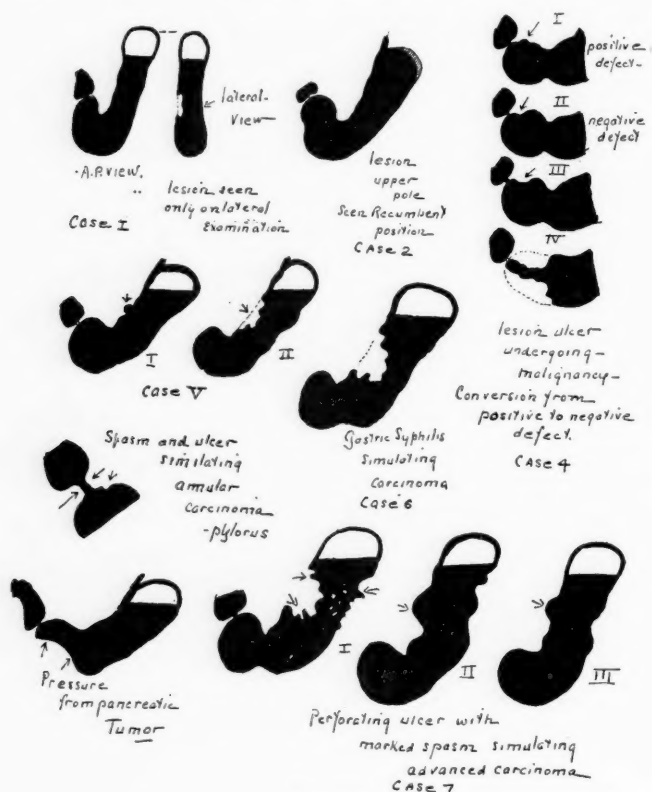


Fig. 132.

there is no recognizable alteration in the contour of the stomach on x-ray examination, and no alteration in gastric work as revealed by gastric analysis. This is one point militating against early diagnosis, but the most important point rests with the patient—he fails almost invariably to consult the physician until



the disease is well established and often irremediable. Only propaganda can offset this difficulty. The early diagnoses have often been made by accident in a general survey of a patient, or it has often been made in those cases where a diagnosis of an organic disease of totally different type was suspected.

The *x*-ray constitutes the best method of localizing a carcinomatous lesion in the gastric wall, and the prime requisite is the exact determination and localization of a filling defect. Carman, that master of palpatory technic under the screen, points out that 95 per cent of gastric cancers give *x*-ray evidence of their presence. Taylor and Miller, in an analysis of 182 cases at the University Hospital, found that the *x*-ray gave a positive diagnosis in 96.8 per cent. of cases. In only 1 case was it misleading. And the general consensus of opinion is that about 95 per cent. are recognizable by this means. If, therefore, it follows that 19 out of 20 are definitely ascertained in this way, either this method of examination is being delayed or in the hands of inexpert observers. I propose in a short résumé of a few illustrative cases to point out some of the difficulties:

**Case I.**—Woman of forty-eight sent to me with a diagnosis of infected gastritis with positive intubation evidence of a malignant lesion, but *x*-ray evidence, according to her physician, that there was no lesion in the gastric wall. I had the advantage of studying this woman three months after the first analysis was made. On intubation we found pus, blood, and anacidity not only during the interdigestive phase, but with a test-meal. This is only found in one of three chronic diseases of the stomach—carcinoma, syphilis, and infection of the gastric wall. Her Wassermann was negative and she was prepared for *x*-ray examination. On fluoroscopic examination in the usual position her stomach was entirely negative. I noticed some peribronchial thickening of a rather compact nature to suggest metastases, so I persisted and finally found on lateral examination a rather flat sharply shelved lesion squarely on the posterior wall. As she was a rather large woman the palpatory "lacune" which can be demonstrated in these patients in anteroposterior examina-

tion was not present. Since this instance *I have examined every patient not only in the anteroposterior but also the lateral position and have encountered this finding in 3 other cases.* Another point is the fact that when x-ray findings and gastric analysis disagree, the fault is usually the observers.

**Case II.**—Mr. H., aged forty-four. This case is the instance of another mistake; the patient having been x-rayed was then submitted to operation, with negative findings. Continuing to lose weight and strength, I was called to see him, and all the evidence of his case presented. The only important point seemed to be an irregularity in the region of the air chamber. I insisted on fluoroscopic him again. In the recumbent position it was apparent that there was an irregular infiltration in the upper pole of the stomach, but not involving the cardiac orifice. Further examination revealed metastases to the left chest and a pleurisy with effusion. *To me this was one of the most difficult forms to diagnose, inasmuch as there was no evidence of the cascade type of filling seen in cancer around the orifice.* I saw the latter frequently in Europe and several occasions since, but in this instance there was evidently a scirrhus lesion beginning in the dome of the stomach and spreading laterally. Case has pointed out the great value of lateral recumbent posture in studying pyloric defects, and the same holds true of the entire upper pole of the stomach wall. *Since then in all doubtful cases I have also used this method of examination.*

**Case III.**—Mr. T., aged forty-three, emphasizes still another phase of x-ray and clinical examination. This patient lost 37 pounds in three months and suffered constant pain. His gastric acidity ran to 79 total, but free acid only reached 29 with an ordinary Ewald meal; furthermore, his mucosa showed a tendency to bleed rather easily, but in every other respect his findings were negative. His x-ray studies repeated on four occasions were absolutely negative, as was the rest of his tract. He had some resistance in the upper right quadrant and within two weeks took a marked turn for the worse. At that time a vague mass

synchronous with the liver could be felt. Dr. Kennedy operated on him at the Price Hospital and found multiple lesions through the liver and one which gave the palpatory signs, but he found "several indurated areas in the stomach wall." These areas in all probability represented the primary lesion. *On several occasions I have seen minute primary lesions in the gastric wall overshadowed by massive secondary metastases.* I can remember how much worry that case gave me, and I still maintain that apart from the physical finding with no clinical signs of liver disease at that time five years ago the only definite evidence was the gastric bleeding.

**Case IV.**—This teaches a different lesson. It was that of a man aged forty-nine with a long digestive history of over twenty years. Mr. M. had only typical ulcer symptoms for three years previous to his examination in the fall of 1919. Under ambulatory ulcer treatment his symptoms entirely disappeared. A recurrence took place in August, 1920 when I first saw him. At that time he had a very small defect about  $\frac{1}{2}$  inch proximal to the pylorus. I put him in the hospital and he gained weight, and the signs from a subjective standpoint entirely disappeared. I rerayed him shortly afterward and was not satisfied with the result. There was a smooth negative rather than positive defect such as the accompanying drawing shows. I told him I wanted another x-ray opinion, and suggested that he go see anyone he wished, namely, a small group in which I had absolute confidence. He went to see Dr. Pfahler and he recognized the same finding, and told me he thought it might be malignancy. This was also my interpretation and I explained it fully to the patient, urging operation. He refused this absolutely and maintained that he always was able to pull out. The possibility of carcinoma had no terrors for him at that time. Nearly two years later he came back and consented to operation. I x-rayed him again before operation and the entire antrum was infiltrated. At operation he had an extensive carcinoma of the antrum with secondary involvement of the liver. *This experience taught me to always suspect a negative defect in the stomach of*

*whatever nature. A negative defect is as dangerous as a positive broadening of an ulcer niche.*

**Case V.**—Mr. B. is mentioned because, as in Case IV, he represented the conversion of ulcer to cancer. In my experience the incidence of the conversion of ulcer into cancer is about 2 to 3 per cent., and almost always it is a gastric ulcer. I have never seen a duodenal ulcer become malignant, but on three occasions in the last four years I have actually visualized the transition from ulcer into cancer. In two of these the patient absolutely refused operation, only to come to the operation too late, after numerous delays and repeated consultations with various physicians who disagreed. In this case, however, the patient was symptomatically well of what was a typical ulcer of the lesser curvature; three months later he returned with a clean-cut and rather extensive carcinoma in the same place. In this case there was nothing to direct suspicion to such a transformation. I only mention it because it emphasized *the extreme rapidity of transformation and, second, the absolute necessity for watching so-called healed ulcers.* A complete change came over the patient in that time. In another communication I hope to give the details of the above cases which are merely selected at this time to emphasize this point. Apparent clinical improvement unless roentgenographically controlled is one of the most dangerous grounds on which to base recovery. I have seen an individual with gastric carcinoma gain weight on several occasions. One case gained 12 pounds in weight; a recent inoperable gastric cancer gained 5 pounds in weight. There is only one criterion I know, and that is the roentgenogram, and even that may be deceptive. Don't go away for any length of time and leave a case suspicious of carcinoma without instructions for reray in two weeks at the most. My own experience teaches me more and more *to treat gastric carcinoma as an acute lesion and to deal with it in as summary fashion as is humanely possible.*

**Case VI** is mentioned only because it emphasizes a type

from which at times gastric carcinoma is scarcely distinguishable. Mr. C., aged forty-six, vomited food all the time, usually in from one to three hours. He has been losing weight slowly in the last five to six years, but 25 pounds within the last year. Residuum shows no food retention, but T. A. 12, F. A. trace; test-meal shows a curve going to 34 T. A. and only 6 F. A. with blood in every sample. On x-ray examination he had a large irregular defect between the middle and antral thirds of the stomach, so large, in fact, as to appear readily palpable. There was much about this case to suggest its cause, his color and general appearance despite the loss of weight, the soft abdomen, the lack of demonstrable metastases, and the conservation of his appetite, all of which pointed to the only other common lesion simulating carcinoma with such an analysis, namely, gastric syphilis. He had a plus 4 Wassermann and showed rapid improvement under specific treatment. *My rule in every gastric defect is to insist on a routine Wassermann.*

**Case VII** is mentioned because it emphasizes the difficulty in distinguishing between malignant and benign ulcer. Mrs. P., aged sixty-five, was a sufferer from "indigestion" for a long period of time, but with acute exacerbations of persistent nausea and vomiting. My technician, who prides herself on her diagnostic ability, said it was a clean-cut case of advanced carcinoma, and that she found not only anacidity, but the typical coffee-ground material. At the height of digestion her T. A. was 10 and F. A. 0. On making a screen survey I immediately made a diagnosis of an inoperable mediogastric carcinoma, probably adherent to the liver, and informed the family of the diagnosis. I explained the method of treatment and put her on our No. 1 ambulatory ulcer diet with sedatives and antispasmodics. In this case there was diffuse upper abdominal resistance, but no definitely palpable mass, a fact which I explained as being due to a rather small stomach behind the left thoracic cage. To my astonishment the x-ray picture of this case gradually unfolded to that of an extensive penetrating ulcer of the lesser curvature with a rather broad niche, and the moth-eaten ap-

pearance totally disappeared. At last examination all the diffuse infiltrated appearance has entirely disappeared and, to all intents and purposes, the patient is clinically well. She has at present no subjective symptoms, and her family will not consider operation. I am only left one interpretation, namely, perforating ulcer with adhesion formation and extensive spasm. I still believe that this type will, if it has not already become so, develop malignancy. A detailed report with Roentgen pictures should naturally accompany the description of this case, but I have tried to draw an outline of the successive changes as I saw them in the stomach wall. I have repeatedly seen an ulcer niche of the gastric type rapidly disappear, but those due to duodenal ulcer are much more refractory. I mention this case because of the confusion in the picture, and because I was thoroughly convinced that it was that of a large inoperable carcinoma. Years ago I encountered just such a picture in gastric syphilis, but the Wassermann was negative in this case.

Malignant ulcer is a fascinating study to the gastro-enterologist, and there is much to be said on this subject which space prevents. I only know one way to be on the lookout and avoid errors, frequent reray and frequent intubation, and finally the fact that malignant ulcer will continue to show occult blood in the test-meals and stools in spite of the most careful ulcer treatment. In my experience, it is rare to find a positive occult blood reaction after the eighth day of ulcer treatment in any type of case except that undergoing malignant degeneration.

Before leaving this subject of x-ray interpretation of gastric carcinoma one must make reasonably sure of the persistent nature of the defect by reray. Gastrosplasm, either partial or total, may give a very deceptive picture, resembling either a small scirrhus stomach, or, through inducing antrum spasm, produce a picture similar to that seen in infiltration. This is not uncommon in chronic gall-bladder disease. Another difficult picture to interpret is beginning carcinoma at or near the pylorus. I had several cases which for years baffled some of the best radiologists, one of which, Mr. M., from Toledo, Ohio, was

repeatedly diagnosed both for and against carcinoma. Since the first examination, more than five years ago, all signs of his condition have gone away, although the appearance at one time was absolutely typical of an annular carcinoma of the pylorus. Carcinoma of the pancreas and carcinoma of the bowel are two lesions which owing to their general effect on the system often suggest gastric carcinoma clinically, and in which the diagnosis is made only by a careful survey. The defect of pancreatic carcinoma is an external pressure defect, and the gastric analysis of pancreatic carcinoma usually reveals intact gastric function until late in the disease.

The second method of examination is gastric analysis. Gastric analysis is simply the measure of gastric work expressed in terms of secretion and evacuation. Mucosal function is estimated by the quantity and quality of the secretion elaborated, and muscular and sphincteric function are estimated in terms of food chymification and food evacuation. Gastric carcinoma *causes a progressive downward trend in the gastric secretory output*. It is therefore obvious that in the evolution of the development of the lesion there must be a gradual transition from a normal secretory output to the eventual disappearance of acidity. I believe I have seen every form of response from the high acid to the low acid response, and I am convinced that we shall have to recognize this lesion in a stage before anacidity if we can hope for real progress in this line.

What impresses me most, however, is the frequency with which there is a persistence of free acid until the later stages of the disease, and after that the rather rapid appearance of anacidity with all the findings of an infected gastritis, namely, the presence of pus, blood, mucus, and bacteria. The question has often been asked as to whether gastric carcinoma was more frequent in those who were the subject of a benign achylia. Zweig recently reported a series of cases in which this possibility was held to occur in those who showed signs of a progressive atrophic gastritis. In one case of ulcer transformation I was able to follow the downward trend of the secretion, but almost until the last month the secretory output was fairly high.



One of the most important points in the examination of a suspected case of gastric carcinoma is the examination of the fasting stomach. Care should be taken to insist on total abstinence from all food after the meal on the preceeding evening. The complete residuum is then extracted by means of the fractional tube. In order to guard against the possibility of traumatic bleeding the tip of the tube can be dipped in paraffin, taking care to see that the tip is patulous. The residuum is then examined for microfood retention, pus, blood, and acidity, and a microscopic examination is made of the material. There are three common findings in gastric carcinoma. Microfood retention, occult and even macroscopic blood, and pus. Many of these cases show in their earlier stages no such findings as coffee-ground vomitus, but digested blood in traces is not uncommon. I have frequently seen all the mucopurulent and bleeding evidence of a lesion completely disappear after regular lavage. In one case which I saw six years ago, and incidentally the patient who gained 12 pounds in weight under treatment, I learned this important lesson. When I first saw him he was the typical picture of a fairly well-advanced carcinoma with a palpable mass and marked weight loss. He had a large lesion extending downward from the lesser curvature, and only indirectly blocking the pylorus; and he complained of constant pain and distress and inability to eat. The first analysis revealed a fetid, dirty, bloody, mucopurulent mass which is seen in so many cases of advanced carcinoma. He experienced so much relief from the removal as well as the test lavage which followed that I thought it advisable to continue lavage. In three weeks he was markedly better, was eating again, and started to gain weight rather rapidly. The most impressive point to me was the almost complete disappearance for a short period of time of the evidence of secondarily infecting factors giving rise to mucus. I have seen cases where the presence of these findings was not recognized in true gastric carcinoma, but they are relatively rare. Bennett in a recent communication discusses this same subject. He gives charcoal on the night previous, and then by careful extraction with the small tube attempts to demonstrate



its presence on the following morning. He found 30 out of 53 cases of gastric carcinoma revealed the presence of charcoal on the following morning. There was present either a foul odor, lactic acid, or a relatively high concentration of acids other than hydrochloric acid in 20 of the remaining 23 cases. In other words, evidence of minimal motor stagnation, reduction in acidity, evidence of congestion or erosion of the mucosa by the presence of bleeding, fermentation with the development of organic acids, and finally, pus from the presence of secondary infection. It is sometimes difficult to differentiate gastric pus from swallowed pus in the gastric contents. As a general rule swallowed pus is discrete, aerated, associated with epithelia from the mouth or upper air passages, while gastric pus is usually present in the form of a veritable purée of leukocytes throughout the material. Furthermore, the presence of pus and blood in the lavage with salt solution after the removal of the residuum is suggestive.

In the study of the stomach in response to a test-meal one must select a meal of great simplicity in order that any pathologic exudate will be readily detected. The Ewald meal readily fulfils this indication, and if there is anything besides the meal and the gastric secretion in the material extracted its presence must be explained.

Gastric carcinoma may reveal itself in one of the following ways:

1. It produces a definite downward trend in the gastric secretion with, as the commonest types of response, a general subacid, delayed secretory, or anacid curve.
2. There is an increase in combined acidity and usually a disproportionate decrease or disappearance of free acidity.
3. There may be a motor delay; in some cases, like diffuse scirrhus involvement of the pylorus and antrum, the evacuation time may be unduly rapid; in other cases, and by far the greatest number, it is delayed.
4. There is not infrequently a minimal delay with microretention where the bulk of the meal has left the stomach in unduly rapid fashion. (I was impressed with this finding in one case of carcinoma of the body of the stomach. In that case the evacua-

tion time was less than two hours, but in even four and six hours later traces of food and thin mucoid secretion was obtained.)

5. The carcinomatous stomach is prone to bleed on slight provocation. This is also true of gastric syphilis, and infected gastritis. Blood is liable to be hemolyzed and indicates congestion or erosion of the mass.

6. Unaërated diffuse mixed pus throughout the entire gastric response is the most direct evidence we possess of gastric infection. It is found in only the three conditions mentioned above. In the cancer there is a positive defect on the x-ray picture and usually a negative Wassermann; in syphilis there is both a defect and a positive Wassermann; and in the infected forms of gastritis there is neither a defect on the screen nor a positive Wassermann.

7. There is usually in well-marked carcinoma an increase in soluble protein which increases as digestion proceeds. Clarke and myself some years ago studied this phenomenon and were impressed by the fact that in carcinoma there is a tendency to a slow increase in the protein of the gastric contents over and above that found in normal controls. Not only the increase, but the gradual development of this increase, is characteristic of carcinoma as contrasted to the sudden increase in hemorrhage.

8. Wiener has pointed out the value of the estimation of the total chlorin of the gastric contents in differentiating carcinoma. According to this observer the chlorin contents of the gastric contents varies from 0.199 to 0.44 per cent. and never exceeds the chlorin content of the blood-plasma. In gastric carcinoma it can be apparently much higher. In gastric carcinoma with low values for the chlorin in the form of hydrochloric acid high total chlorin (0.34-0.58 per cent.) is important. He explains the high total and high combined Cl in carcinoma as the result of the destruction from a stretch of normal mucous membrane, the diffusion rate between the gastric contents and the lymph tracts is changed, and more sodium chlorid flows than in benign achylia.

I believe that the idea of anacidity as a characteristic feature

of gastric carcinoma is a false one. I have seen many cases in which there is no anacidity. Hartman of the Mayo Clinic made a careful statistical study of 551 cases of gastric carcinoma and 80 cases of carcinomatous ulcer operated upon at the Mayo Clinic from 1918 to 1920. He found that achlorhydria was found in a little less than one-half the cases of carcinoma. Normal or hyperacid findings can be expected in more than one-quarter. In gastric analyses studied without reference to the lesion, 53.72 per cent. or about one-half of the patients only had anachlorhydria; 15.78 had free hydrochloric acid in small amounts; in 17.42 per cent. the gastric acidity was normal; and 4.58 per cent. had hyperacid figures. He also mentions the occasional marked difference in total and free acidities, seen particularly in pyloric lesions. In malignant ulcer only 22.5 per cent. had hypo-acid values, and 72.5 per cent. showed acidity of various grades. The persistent presence of occult blood in the feces or gastric contents is found in about 80 per cent. of all cases. If an ulcer is submitted to medical treatment and the occult blood does not disappear from the feces in the second week, it is suspicious of malignant degeneration and should be rerayed.

Apart from the history and physical signs I like to balance the x-ray findings with those obtained by gastric analysis. If these fail to agree, there may be some other explanation for the trouble, but it is of rather rare occurrence that one or both of these methods will not reveal the presence of this insidious lesion.

In reviewing this subject I have the following suggestions to offer: Roentgenologic examination:

1. This should include careful fluoroscopic study not only in the anteroposterior position, but the lateral one as well, so as to disclose lesions on the anterior and posterior wall.
2. An examination in the recumbent position is necessary in all doubtful cases to reveal lesions in the cardia as well as to more perfectly visualize the pylorus.
3. A small diffuse gastric lesion may fail to reveal its presence on x-ray examination, but in 95 per cent. of cases the lesion gives roentgenologic evidence of its presence.

4. Always suspect a negative defect in the stomach even though it has the dimpled appearance of healed ulcer.

5. Carcinoma of the stomach ought to be treated like an acute lesion.

6. Healed gastric ulcer ought to be repeatedly rerayed owing to the possibility of malignant transformation.

7. A routine Wassermann should accompany the demonstration of every gastric defect.

8. Sins of commission as well as omission can occur, and where a reasonable doubt exists only repeated reray and complete and exhaustive study may enable one to reach a conclusion.

Regarding gastric analysis:

1. Examine the fasting residuum for retention, microretention, pus, blood, and organic acids. These are the cardinal points in that study.

2. Use a simplified test-meal, preferably the Ewald meal, which will reveal pathologic exudates.

3. A tendency to generally lowered acid output up to total achlorhydria, the presence of increased soluble protein, the presence of organic acids, a tendency toward the reduction of free hydrochloric acid, and an increase in combined acidity, the presence of an increase in total and combined chlorin, the demonstration of gastric pus and blood throughout the digestive period, are the important points to be sought.

4. It is now generally acknowledged that in a large proportion of the cases of gastric carcinoma hydrochloric acid is still present, and in the majority of cases of malignant ulcer it reaches a fairly high level.

5. The search for evidence of a congestive, ulcerated, infected lesion is usually performed through a consideration of other factors than acidity.

6. An attempt should be made to correlate these two methods of study in view of the fact that they answer different questions. The x-ray answers the questions as to form, position, mobility, and alterations in contour, while gastric analysis points out the alterations in gastric work and the evidence of exfoliation or exudation of pathologic products from the diseased area.

## CLINIC OF DR. GEORGE W. NORRIS

PENNSYLVANIA HOSPITAL

### A CARDIAC CASE FOR DIAGNOSIS

THE patient whom I present to you today, an American by birth, forty-seven years of age and one of our hospital orderlies, was admitted a few days ago complaining of severe pain in the lower chest and upper abdomen. While carrying two large buckets of coal upstairs he was suddenly seized with agonizing pain so severe that he dropped the buckets and lay down. The pain lasted thirty minutes; it was paroxysmal in character, caused him to grasp his abdomen, but was unassociated with gastro-intestinal symptoms, dizziness, or dyspnea. It radiated upward into the left chest and along the left trapezius muscle. It was not noted in the arm. When the pain was over he was completely exhausted and was carried to bed. Ten hours later the pain recurred and was associated with loose bowel movements.

Since the onset three days ago paroxysms of pain have occurred with increasing frequency. They bear no relation to meals and appear spontaneously without evident cause. In some of the attacks gaseous eructations are a prominent feature. There is no cough or expectoration and breathing is not affected. He has never had any evidence of heart disease other than very slight dyspnea on exertion.

**P. M. H.**—The only data of importance are an attack of "indigestion" with belching of gas and discomfort after meals six months ago. This attack was readily relieved by treatment and he attributes it to overeating, especially of meat. He does not use alcohol or tobacco.

**P. E.**—Temperature 102° F., pulse 96, respirations 28. Adult

male with ashen gray pallor, obviously in pain and apparently seriously ill. He now complains also of pain in the lower jaw and over the left mastoid region. All of the regions where pain is felt are acutely tender to the touch. There is marked pyorrhea, moderate distention of the veins of the neck. Expansion of the left lower chest seems less than over the right. Marked pulsation is visible in the carotids, in the episternal notch, and in the epigastrium. *Heart*: Apex impulse, which is heaving, 12 cm. from midsternal line—fifth interspace. Dulness extends  $12\frac{1}{2}$  cm. to left,  $2\frac{1}{2}$  cm. to right of midsternal line. Postmanubrial dulness 7 cm. There is a double aortic and double mitral murmur. *Lungs*: Negative except for a few crepitant râles at the bases. *Liver*: Just palpable in the epigastrium. The *abdominal aorta* which pulsates actively and expansively seems increased in width and over it a loud systolic murmur is heard.

**Special Examinations.**—*Urine*.—Acid, 1020–1028, trace of a cloud of albumin, no glucose, occasional hyaline casts.

*Blood*.—Hemoglobin 75 per cent.; reds 3,840,000; leukocytes 16,700, of which poly. 64; L. L. 5; S. L. 28; Tr. 3. *Blood Wassermann*: C + 3; A + 4.

*x-Ray of Chest*.—There is a questionable slight enlargement of the shadow of the aortic arch, but no definite aneurysm.

*Blood-pressure*: 130/40; marked sclerosis and tortuosity of the superficial arteries; distended superficial veins and the usual peripheral pulsating phenomena of late aortic insufficiency.

For several days the patient suffered greatly and morphin in large doses was required to make him even reasonably comfortable.

As you see him today he has almost recovered symptomatically, although he still at times has in minor degree a return of pain. Of the fact that this patient is suffering from a serious organic and probably dangerous lesion, both the history and still more so the appearance—ashen pallor, anxiety, restricted and painful breathing—indicated. What are the etiologic possibilities?

The following conditions certainly must be considered: (1) Coronary thrombosis. (2) Angina pectoris. (3) Aneurysm. (4) Gall-stones. Let us consider these serially.

1. **Coronary Thrombosis.**—This condition is far commoner than was until recently supposed. Formerly regarded as inevitably and quickly fatal, we now know that the coronary arteries are not end arteries in the strict sense which we were formerly taught to believe. Gross has shown that varying degrees of anastomosis are quite usual and we know that a certain collateral circulation may actually be developed if a small branch is involved. The likelihood of the establishment of a collateral circulation seems to vary directly with the slowness with which occlusion has occurred. These facts doubtless explain the marked (at least temporary) benefit which sometimes follows prolonged rest in bed which is seen in some cases of "angina pectoris."

An attack of coronary thrombosis can often be recognized by the following characteristics: The onset is abrupt, agonizing, and alarming. It may occur at the first manifestation of heart disease or may appear as a culmination in a patient who has previously shown evidences of restriction in his cardiac reserve—dyspnea, fatigue, palpitation, or precordial oppression on exertion—if not actually some signs of decompensation.

The first manifestation is a sudden, piercing or boring, excruciating and enduring pain of cardiac distribution (epigastric, substernal, hypochondriac, or precordial), with radiation to the neck, arm, nipple, or abdomen. Not infrequently the attack follows a heavy meal, and when the pain occurs in the epigastrium is mistaken for acute indigestion.

Associated with this is usually dyspnea, weakness, ashen pallor, and agony. The pain, unlike that of angina pectoris, does not pass off after a brief interval. Other manifestations, such as cough, sweating, cyanosis, nausea, vomiting, diarrhea, delirium, aphasia, collapse, or coma may occur. The attack may, but frequently does not, follow exertion or eating.

If definite evidences of cardiac decompensation existed previously the onset of the thrombosis tends to be marked by sudden exacerbation or superaddition to symptoms already present. Dyspnea, cyanosis, pain, etc., increase, or the patient becomes suddenly pale, collapsed, or irrational.

The pain of coronary thrombosis may diminish, only to be renewed by cyclic exacerbations. It is unrelieved by postural change and responds far less to morphin and local measures, such as counterirritation and blood letting, than do simulating conditions. Dyspnea may overshadow the pain, a dyspnea for which neither the physical findings in the lungs nor in the heart seem to offer an adequate explanation. The respirations are shallow and vital capacity in the cases studied markedly decreased (Wearn).

In severe cases pulmonary congestion and edema are constant findings, regardless of whether the right or the left coronary arteries are obstructed.

Vasomotor changes are marked. The typical facies is anxious, suffering, and ashen gray.

If the patient survives the first twenty-four hours polynuclear leukocytosis and a fever ( $100^{\circ}$  to  $104^{\circ}$  F.) are frequently noted. These findings are explained as resulting from the absorption of "foreign protein" from the necrotic heart muscle.

Urinary findings vary with the degree of renal arteriosclerosis or nephritis previously present.

Electrocardiographic findings are variable and in nowise characteristic.

Sudden death may occur and be variously attributed to "acute indigestion," angina pectoris, or angina abdominalis. Such an abrupt termination appears to be more common in those in whom no heart disease had previously been recognized.

On the other hand, the patient may live for days, months, or years. Such instances verified by necropsy have been reported by Herrick. As a rule, however, the patient survives the first attack only to be carried off by a subsequent one in the not distant future.

**2. Angina Pectoris.**—This relatively common ailment of brain workers is characterized by sudden, agonizing epigastric or substernal pain often with radiation to the neck and arms. The pain is usually induced by exertion or digestion—often in combination—it lasts from a few seconds to a few minutes. It produces instant arrest of muscular activity, often even of breath-



ing, and is associated very commonly with a premonition of death—a sense of impending dissolution. In other words, the term “angina” is applied to heart pain, occurring in paroxysms—severe and more or less typical in character—and frequently and suddenly fatal. It is best to reserve the term “angina pectoris” for this type of case.

As I have already indicated heart pain of lesser degree occurs commonly in many conditions. The athlete may have it to some extent after a long race. The patient with acute or chronic heart disease may similarly experience it. Its distribution, even to radiation down the ulnar distribution of the forearm and hand, may likewise be observed. These cases may be described as anginoid if by this you simply describe a heart pain. But the term “false angina” is objectionable. True angina is a reflex pain arising from a diseased aorta—coronary sclerosis or occlusion may or may not accompany it.

Is our patient suffering from angina pectoris? I think not. The attacks last too long, recur too frequently and are, except the initial one, too unprovoked.

3. **Aneurysm.**—The pain may readily be explained as a result of aortitis. The patient has active, presumably long-standing syphilis. Our first thought was aneurysm of the aortic arch, but x-ray studies have failed to disclose any abnormality of contour in the course of the aorta above the diaphragm. But below the diaphragm? The radiologist “sayeth not.” Remember that we found a fairly large rounded expansile pulsating mass in the left epigastrium quite in keeping with what one might expect in a small aneurysm of the abdominal aorta.

Aneurysm may cause acute pain by pressure on sensitive structures or by increasing extension in its own structure. Sudden stretching of an aneurysmal sack—rupture—and the “dissecting” variety are often excruciatingly painful. Rupture can now be excluded because life remains. Dissecting aneurysm chiefly occurs in the descending thoracic aorta and has, we feel, been excluded.

4. **Gall-stones.**—One of the commonest diagnostic stumbling-blocks is gall-stones. These may cause sudden, excruciating

pain, associated with syncope or collapse and radiating to the scapula, shoulder, and neck. Many a case of angina pectoris is—because he has epigastric pain, because he belches gas and is relieved by it, and because his attacks occur after heavy eating—diagnosed gall-stones; and subsequently dies of “acute indigestion.”

As we first saw this man speechless, pallid, and immobilized by pain, no positive opinion was justifiable. Our first impression was either ruptured aneurysm or coronary thrombosis. Today the latter is much less likely and the former can be dismissed.

As I see it, this man has syphilitic arterial disease. He has an abdominal aneurysm and doubtless disease of his aortic arch. The coal buckets were too much for him. His blood-pressure was raised unduly and something gave way. It may be that the arch began a widening process which will in time develop into an aneurysm, or it may be that his abdominal aneurysm became larger through yielding of the arterial coat. Both the pain and the patient's appearance might be explained by the former hypotheses, especially in conjunction with the latter.

## CLINIC OF DR. ELMER H. FUNK

### JEFFERSON HOSPITAL

#### CONGENITAL DIAPHRAGMATIC HERNIA

HERNIA of the diaphragm consists of a protrusion of abdominal contents through an opening in the diaphragm. It should not be confused with *eventration* of the diaphragm, a congenital defect of development in which the diaphragm remains intact but in an elevated position. Nor should it be confused with *evisceration* of the diaphragm, in which that structure is torn by violence, abdominal contents finding their way into the thoracic cavity or, rarely, thoracic organs protruding into the abdominal cavity. In hernia of the diaphragm of congenital origin the opening is the result of aplasia of a portion or complete absence of the diaphragm, or a preformed opening, usually the esophageal, is unusually large allowing intrathoracic protrusion of abdominal contents.

In the development of the diaphragm the striated muscle portion takes its origin from a pair of premuscle masses which in early embryonal life originate opposite the fourth cervical segment. These muscle masses migrate caudally and fuse with the pleuroperitoneal membrane which grows from the dorso-lateral part of the body wall, thus separating the pleuroperitoneal cavities. Defects in the dorsal part of the diaphragm are more common than defects in the ventral part of the diaphragm. The persistence of a dorsal opening in the diaphragm, most commonly on the left side, is the result of an imperfect development of the pleuroperitoneal membrane. Apart from the gaps due to the failure of fusion and the dilated preformed openings, hernia may occur as the result of the bulging of weak areas. Such areas exist posteriorly at the junction of the costal and lum-

bar portions, and anteriorly at the junction of the costal and sternal portions of the diaphragm (acquired hernia).

In congenital diaphragmatic hernia the protrusion may be present at birth or not occur until years after. When the protrusion occurs after birth an injury wholly without effect on an intact diaphragm may determine the entrance of the abdominal contents into the thorax. It is an interesting question, clinically, when hernia is evident later in life whether the hernia is con-



Fig. 133.—Congenital hernia of the diaphragm (Downes, Surg., Gynec., and Obstet., 393, October, 1918).

genital or acquired. It is my opinion that if one excludes evisceration or true traumatic hernia the remainder of the cases fall into the group of congenital defects of the diaphragm, whether such defect be evident at birth or not for some years afterward. Congenital diaphragmatic hernia occurs most frequently on the left side. Hume<sup>1</sup> collected from the English,

<sup>1</sup> Brit. Jour. of Surg., 1922, 10, 207.

French, and American literature 35 cases of undoubted congenital diaphragmatic hernia reported between 1910 and 1921. In this group there were 18 cases of hernia through the left dome, 12 cases of hernia through the esophageal orifice, 4 cases of absence

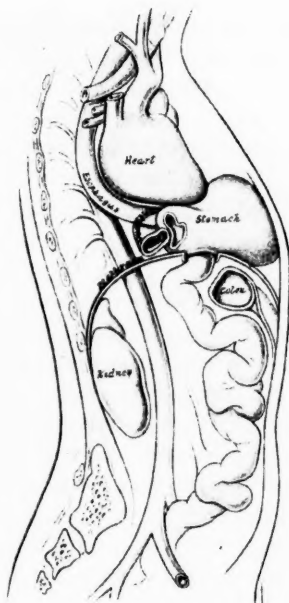


Fig. 134.—Diagrammatic sagittal section of congenital hernia of the diaphragm (Downes, Surg., Gynec., and Obstet., 393, October, 1918).

of the left diaphragm, and 1 case of hernia through the hiatus pleuroperitonealis.

#### PRESENTATION OF PATIENT

Mrs. R. M., aged twenty-five years, was admitted to the Jefferson Hospital complaining of cough, expectoration, loss of weight and strength. The *family history* reveals that her father died at sixty years of age of chronic bronchitis (?) and one sister at present has a cough of some years' duration. The

patient's *past personal history* reveals "marasmus" in infancy and pneumonia in early childhood. In 1919 a mild attack of influenza occurred. Two years ago she married a man in poor health. His mother died of tuberculosis about the time of marriage. The patient had some transient contact with her mother-in-law. One year after marriage a child was born. This child subsequently died at the age of eleven months of abdominal tuberculosis. No history of injury. The *present illness* began three years ago following an attack of bronchitis. The cough continued, with gradual loss of weight and strength. Following the pregnancy mentioned above these symptoms became more marked. When admitted to the hospital the cough was quite distressing and productive of a moderate amount of yellowish sputum. No hemoptysis has occurred. Substernal soreness is present in varying degree from time to time, but at no time has acute pain been present anywhere in the chest. In the afternoon she feels feverish and occasionally night-sweats occur. Her best weight was 113 pounds, her present weight 95½ pounds, a loss of 17½ pounds during the past three years. There has been no hoarseness or dyspnea. The appetite is fair and the bowels are regular. The menses are normal.

The *physical examination* reveals an emaciated, pallid female. No dyspnea or cyanosis is evident. The examination of the eyes, ears, nose, and throat reveals nothing abnormal. The teeth are in bad condition and pyorrhea is present. There are numerous small glands palpable in the anterior cervical region. The *chest* examination reveals some striking findings. The chest wall shows wasting, the sunken spaces above and below the clavicles are exaggerated, and the bony framework is unduly prominent. There is distinct limitation of movement on the entire left side. This is confirmed by palpation. If one observes especially the inspiratory movement of the costal margins of the subcostal angle it will be noted that the left side is fixed. Keep this in mind, since it helped us in arriving at the correct diagnosis. Percussion reveals a dull note with a tympanitic element (boxy tympany) above and below the right clavicle, hyperresonance throughout the remainder of chest except in

left axilla, where the note is distinctly tympanitic. Auscultation over the right chest reveals quiet breath sounds with prolonged expiration and many fine crackling râles from apex to third rib anteriorly and to about the level of the fifth rib posteriorly. Auscultation over the left chest reveals nothing abnormal of note at the top of the lung, but below the fourth rib the breath sounds and voice sounds are suppressed and an occasional splashing sound or gurgling sound is heard. We did not hear this sound at the time of our first examination. It is readily recognized as the sound which one hears over the stomach after the ingestion of fluids. She has just taken a pint of milk. The *apex of the heart* is felt in the fifth interspace about 7 cm. to the left. The left border of cardiac dullness cannot be determined with certainty, the right border is at the right border of the sternum. The heart sounds are distinctly audible. No signs of cardiac disorder can be elicited. The *abdomen* is somewhat flattened, but otherwise normal in contour. The *liver* dullness is normal. The *spleen* is not felt and splenic dullness cannot be made out. No masses are palpable. The extremities, except for evidences of emaciation, reveal nothing of note. There is no clubbing of the fingers.

**The Problem of Diagnosis.**—The salient points in the history and physical examination are tuberculosis contact, local and general symptoms suggesting active pulmonary tuberculosis, signs of infiltration in the upper part of the right lung, and signs at the left base which suggest for differentiation pneumothorax, large cavity in the lung, eventration of the diaphragm, diaphragmatic hernia, distended stomach or colon, and localized emphysema of the lung such as occurs when an organic foreign body obstructs the left lower lobe bronchus.

**Pneumothorax.**—The presence of tuberculosis is verified by the finding of tubercle bacilli in the sputum. Since pneumothorax is a common complication of tuberculosis, it requires first consideration. There is an absence in this patient of the usual history of sudden onset of pain in the side with dyspnea and cyanosis which characterize pneumothorax. It should be recalled, however, that a fairly large pneumothorax may develop

insidiously and remain latent as far as symptoms are concerned. We cannot, therefore, rule out pneumothorax on the symptomatology. The heart is not displaced and this finding is against pneumothorax. The gurgling sound heard on auscultation is distinct from the metallic tinkle and splashing sound which one hears in pneumothorax with fluid. It resembles that which we hear when auscultating over the abdomen. It becomes quite pronounced after the patient ingests fluids, and our attention is therefore directed to the possibility of stomach and bowel occupying this area.

A *distended stomach* may give rise to tympany high up in the left axilla. In such a condition the patient is obviously distressed, there is local discomfort, frequently nausea and vomiting, and the abdomen is distended. Such local symptoms were absent in our patient and the abdomen flatter than normal.

*Eventration* of the diaphragm is a congenital condition characterized by an elevated or high position of the diaphragm, which occurs almost invariably on the left side. Although the diaphragm remains intact, the stomach and intestines may become lodged high up in the thoracic cavity and give rise to the signs which our patient presents.

*Congenital diaphragmatic hernia* differs from this condition in that the protrusion occurs through an opening in the diaphragm. The physical signs of the two conditions are frequently considered as identical, with this exception, that in eventration compression of the lung and contiguous structures is absent, while in diaphragmatic hernia compression and displacement of the heart may occur. There is another differential feature which may have some diagnostic value in the future study of these two conditions, and which was impressed upon me when I compared the notes of this patient with those of a case of eventration which I previously reported. You will recall that in this patient there is inspiratory fixation of the left costal margin of the subcostal angle. In the patient with eventration there was exaggerated inspiratory flaring of the costal margin on the affected side. You will remember that when the diaphragm is depressed, or when costophrenic adhesions



exist, the diaphragm is placed at a mechanical advantage in its opposition to the intercostals (which cause flaring of the costal margins) and the costal margin is fixed or drawn inward. The high position of the eventrated diaphragm places it at a mechanical disadvantage and therefore allows of greater flaring than on the opposite normal side. The fixation in the present patient led us to exclude eventration and favor the diagnosis of hernia. In a personal communication from Dr. Hoover, of Cleveland, who has made a special study of the diaphragm, I learn that in his experience a diaphragmatic hernia *per se* does not modify the excursion of the costal movements, and that when restraint of lateral movements is obtained it is probably due to adhesions between the diaphragm and chest wall. I do not wish to stress unduly the value of the movements of the subcostal margin in the differential diagnosis of eventration and hernia of the diaphragm, although in the two patients just mentioned it served to help.

A large basal cavity with tympany is not likely to be confused with the present condition and the absence of amphoric or cavernous breath sounds. Such a cavity in tuberculosis would be invariably associated with signs in the upper portion of the chest; signs which are absent in this patient. An extensive basal bronchiectasis giving rise to basal cavity signs would be associated with fetid sputum and clubbing of the fingers, both of which are likewise absent in this patient. I think that we can rule out large basal cavity without much difficulty.

*Localized obstructive emphysema* occurring as a result of bronchial obstruction by an organic foreign body, such as a peanut, frequently gives rise to tympany and suppressed breathing. The patients are usually infants or young children, and a history of foreign body inhalation is frequently unobtainable. When occurring on the left side in a child confusion with diaphragmatic hernia may occur. There are, however, the signs of an acute purulent tracheobronchitis with severe general reaction due to septic intoxication. There is displacement of the heart away from the lesion, and the absence of the localized gurgling sounds elicited in diaphragmatic hernia. In our patient.

an adult, the elimination of obstructive emphysema due to foreign body does not offer much difficulty.

I have delayed giving you the x-ray report in order to point out how far it is possible to go without this invaluable, although not always available, aid. Dr. Manges reports that fluoroscopy after an opaque meal reveals a "cavity in the lower portion of the left chest which is seen to be the stomach. It is completely inverted so that the greater curvature points upward instead of downward and the entire stomach is above the level of the diaphragm."

#### THE RECORDS OF THREE OTHER CASES

It seemed to me that it would be interesting to present in connection with this patient a brief abstract of the records of three other patients who were in this hospital during the past seven years.

**Case I.**—S. W., age forty-two years, male, white, salesman, was admitted in August, 1917 complaining of pain in the lower abdomen. His *past personal history* revealed nothing of note. No history of injury was obtained. The *present illness* dated back ten or twelve years, during which time the patient had from time to time pain in the lower abdomen, "sour taste in the mouth and constipation." Four years ago he was operated upon by a New York surgeon, who told him that he had a gastric ulcer, and six months later another operation was performed for adhesions. Since the last operation he has occasionally had mild attacks of discomfort after eating. During the two weeks prior to admission a dull pain was constantly present in the lower abdomen and for the treatment of this he sought admission to the hospital.

The *physical examination* revealed a rather poorly nourished individual with physical signs in the chest suggesting emphysema. The heart was in normal position and the area of cardiac dulness increased. The abdomen showed nothing of note. The temperature, pulse, and respiration were normal during the hospital stay. The gastric analysis, urine, and blood examination re-

vealed nothing abnormal. The x-ray revealed "a hernia of the diaphragm containing stomach and splenic flexure of colon. The gastro-enterostomy *opening* was working satisfactorily. There were no evidences of ulcer or of malignancy." The symptoms of the patient cleared under rest and treatment in the hospital and he was discharged several weeks after admission. This patient had obviously a congenital diaphragmatic hernia diagnosed by the x-ray.

**Case II.**—T. W., age seventy-one years, male, white, produce dealer, was admitted in 1918 complaining of a burning pain in the right upper abdomen radiating to the back and down the right side toward the pubis. The *past personal history* is negative. No history of injury was obtainable. The *present trouble* began four years ago while at work, when he was seized with an attack of vertigo and fell, but was not unconscious. Several hours later the vertigo disappeared and he noticed a burning pain in the right upper quadrant of the abdomen, deep seated and radiating to the back and right lower quadrant. There were no urinary symptoms. The pain was not influenced by the taking of food. Nausea and vomiting were absent. No jaundice was noticed. The pain has continued with varying intensity until admission to the hospital.

The *physical examination* revealed a poorly nourished adult. The notes of the examination by the house officer stated that the lungs were clear. The signs referable to the cardiovascular system were those of sclerosis; the liver was palpable about three fingerbreadths below the costal margin on the right side and midway between the ensiform and umbilicus in the median line; gastric tympany extending high up in the left axilla. The x-ray examination revealed a left-sided diaphragmatic hernia with almost the entire stomach in the thoracic cavity. The temperature, pulse, and respiration were normal during the patient's hospital stay. The clinical diagnosis was that of congenital diaphragmatic hernia suspected before and confirmed by the x-ray. His poor general condition precluded surgical interference and he was discharged one month later and the result is noted as unchanged.

**Case III.**—G. D., age fifty-one years, male, white, machinist, was admitted in November, 1920 complaining of pain in the upper abdomen after eating. His *past personal history* revealed a crushing injury to the upper abdomen and chest in March, 1918 which caused him considerable discomfort for several weeks. His *present trouble* dated back to 1916—four years before admission—when he had what he designates as a mild attack of indigestion which lasted several days. In March of 1920—eight months before admission—he had an acute attack of pain in the epigastric region. He was nauseated, but did not vomit. After this time the attacks of pain would recur with varying severity and usually one to three hours after eating. They would be associated with slight nausea, but no vomiting occurred.

The *physical examination* on admission revealed a fairly well-nourished adult with slight cyanosis. The physical signs in the chest recorded by the house officer were those of emphysema with bubbling râles at the left base. From the record it would seem that the diagnosis was not made until the x-ray revealed the diaphragmatic hernia. The stomach was found to be inverted and the greater portion of it above the diaphragm. The hernia also contained transverse colon and a part of, the mesentery. During the hospital stay the pain and discomfort in the upper epigastrium following eating disappeared under treatment, and the patient was discharged three weeks later to return to his home. He was readmitted to the hospital seven months later, that is, in June, 1921, because of the development of nervous symptoms which were found to be associated with early paralysis agitans. He had had no return of gastro-intestinal disturbance since the previous discharge from the hospital. A second x-ray revealed the same condition as upon the first admission.

*Comment.*—It is of course difficult to determine at this time the relationship of the trauma to the development of the hernia. As I recall from my memory of the patient the history which he gave of the injury and of the symptoms that followed led us to feel that true traumatic hernia or evisceration did not occur at the time. That the injury may have determined the entrance

of abdominal contents through an opening of a congenitally defective diaphragm is entirely possible. It is also conceivable that the injury had no relationship. In this patient, only, of the 4 cases here considered, does the factor of trauma play any part in the etiology, at least as far as one is able to obtain such a history from the patients.

#### DISCUSSION

Although considerable difficulty attends the interpretation of the physical signs of hernia, the x-ray examination after an opaque meal renders the diagnosis, as a rule, easy except in the smaller hernias where barium may fail to fill the herniated portion, or the portion itself at the time of the examination may not be herniated (Soresi<sup>1</sup>).

It is stated that before the advent of the x-ray the diagnosis was seldom made during life. Struppler<sup>2</sup> collected 500 cases in 1901. Giffin<sup>3</sup> in 1912 found references to 145 additional cases, making approximately 650 cases reported to 1912. Only 15 cases were diagnosed correctly during life. I quite agree with Giffin who states that many mistakes have been due to the fact that the physician was unprepared for the condition; that the symptoms and signs were often quite clear, but were not elicited because of lack of familiarity with them. It must be emphasized, and without detracting one iota from the value of the x-ray as a diagnostic adjunct, that many of the failures in physical diagnosis in recent years have been due to a lack of appreciation of the value of the simple methods of inspection, palpation, percussion, and auscultation. With proper attention to the technic of physical examination will come an increased recognition of what were formerly considered rarities of diagnosis, such as diaphragmatic hernia.

The symptomatology is most varied. In many cases the children are stillborn, or death occurs shortly after birth. In the latter group dyspnea, cyanosis, and convulsions are not uncommon.

<sup>1</sup> Annals of Surgery, 254, March, 1919.

<sup>2</sup> Deutsch. Arch. f. klin. med., 1901, Bd. lxx, S. 1.

<sup>3</sup> Annals of Surgery, 1912, 55, 388.

mon. In other instances the condition is latent and discovered only during the course of a routine examination for some other condition. When symptoms are present they may be referred to the chest or the abdomen, or both. Palpitation was the only symptom complained of by one patient reported in the literature. Dyspnea and cyanosis have been noted. Gastrointestinal symptoms are of frequent occurrence, suggesting pyloric obstruction, peptic ulcer, intestinal obstruction etc. Rowlands<sup>1</sup> reports the case of a patient nineteen years old whose symptoms suggested gastric ulcer. He was operated upon and no ulcer found, and the condition of his diaphragm not being suspected, the abdomen was closed without further operative interference and without relief of the symptoms. In a subsequent study the hernia was discovered and a corrective operation performed, with recovery and relief of symptoms. In Bythell's<sup>2</sup> patient, a thin, ill-nourished boy of nine years, recurring attacks of vomiting suggested a diagnosis of pyloric obstruction. Even after the x-ray examination the diagnosis was not clear at first, although diaphragmatic hernia seemed most likely. At operation the major part of the stomach was discovered protruding into the thorax through the esophageal opening. In the case reported by Portis and Portis<sup>3</sup> the clinical manifestations resembled Hirschsprung's disease. The toxemia during the constipated stages with accumulation of feces in the colon was relieved by forced evacuation from time to time of large amounts of fecal material. The x-ray after a barium meal revealed stomach and splenic flexure of colon in a hernia pouch of the left diaphragm. Matthews and Imboden<sup>4</sup> report an interesting case of congenital hernia in a multipara aged fifty-five years who was stout and in good general health. The hernia was unusual in that the protrusion was through an enlarged esophageal opening and the stomach was almost entirely in the right chest. It is conceivable that with the

<sup>1</sup> Guy's Hospital Reports, January, 1921.

<sup>2</sup> Brit. Jour. Dis. Child., 1915, 12, 236.

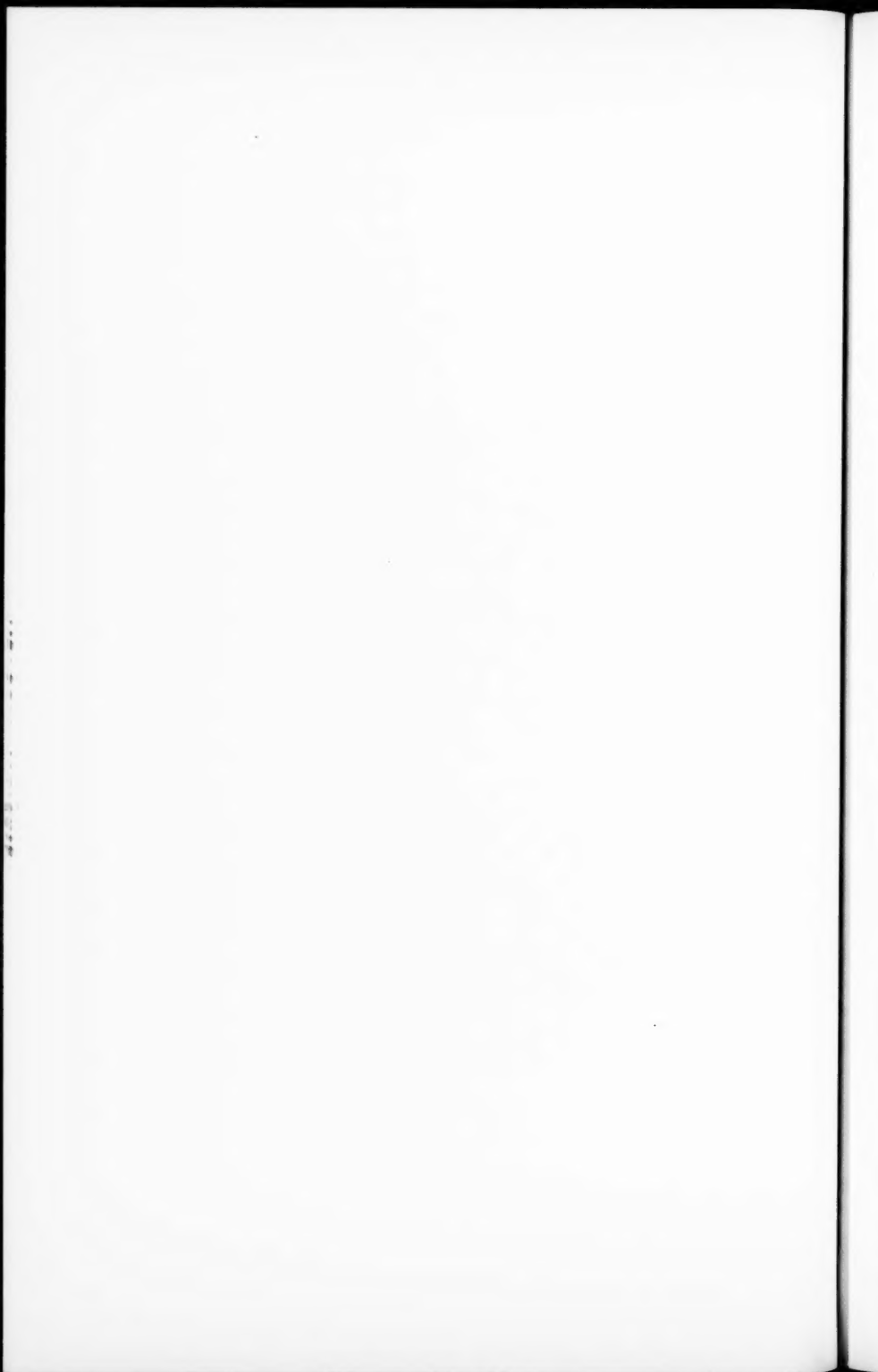
<sup>3</sup> Jour. Amer. Med. Assoc., 1920, 75, 1262.

<sup>4</sup> Ibid., 1919, 73, 267.

increased intra-abdominal pressure incident to pregnancy or tumor the protrusion of abdominal contents through a congenitally defective diaphragm may be aided. As an illustration of the diversity of the symptoms which may occur the case of Soresi<sup>1</sup> is interesting. The patient was a girl of nineteen years of age with dysmenorrhea, constipation, indigestion, and severe abdominal pain. She was operated upon and a right ovarian cyst was all that was found. This was removed, but her symptoms continued. Later she was operated upon again by Soresi and the diaphragmatic gap found and closed, the patient recovering and her symptoms disappearing.

The **treatment**, when such is indicated, is surgical. Ideally, it is desirable to restore the hernia contents to the abdominal cavity and close the opening in the diaphragm. This will be impossible where there is complete absence of the diaphragm, or in those instances where the gap is large; and extremely difficult, if not impossible, when the protruding viscera become adherent and fixed in their abnormal position. Downes points out that in the majority of reported cases it has been possible to restore the organ, or organs, to the abdominal cavity and close the opening of the diaphragm. He reports a case in which it was found impossible, or at least unwise, to attempt reduction, and performed a gastro-enterostomy. The symptoms of obstruction in this case were entirely relieved by the operation. In the patient whom I have presented in this clinic an operation will not be recommended. First, because an active tuberculosis precludes any but an emergency operation, and second, because of the symptomless character of the hernia. This opinion is shared by the surgical consultant.

<sup>1</sup>Annals of Surgery, 254, March, 1919.





## CLINIC OF DR. HENRY D. JUMP

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### ESSENTIAL HYPERTENSION

ESSENTIAL hypertension is a disease in which blood-pressure is increased and in which there is primarily no distinctive pathology or known cause. It is a well-known fact that arteriosclerosis and nephritis are followed by increased blood-pressure, but it is not so generally recognized that hypertension may be the *primary* condition which, in turn, will produce pathologic changes in the vessels and kidneys. There are those who claim that all high blood-pressure is an early symptom of arteriosclerosis or nephritis.

Essential hypertension is usually benign and subject to relief, but, on the other hand, consequences may follow rapidly and extensive damage occur. The following case is shown as an example of the disease.

The patient whom we have before us is a woman of forty, married for twenty-three years, has 2 children and has had no miscarriages. She is employed as a bookkeeper. The chief complaint is *fatigability*. She has had a tendency to become melancholic, but since all devitalized teeth were extracted several years ago has been free of this. She is still *excitable, irritable*, and somewhat *apprehensive*. She works moderately hard under considerable strain and fatigues inordinately. Occipital headaches occurred frequently formerly, but she has had none for six months.

Light attacks of *vertigo* on change of position have occurred lately. There are no flashes of light in the eyes, tinnitus, cough, or pain in the chest. *Dyspnea* and cardiac *palpitation* occur with light exertion, as on going up one flight of stairs. There

are no digestive symptoms except constipation, which is easily controlled. The weight, which is above normal, has remained stationary for several years. Her menstruation is normal: there is no nocturia or dysuria; urine is passed three or four times a day, totaling about 1500 c.c. She sleeps normally and restfully.

Her **previous history** includes measles and frequent attacks of follicular tonsillitis, three attacks of corneal ulcers in the past three years, one mild attack of melancholia as noted above.

The **family history** shows her mother, whom she resembles, died insane at fifty. There has been no other insanity, no nephritis, tuberculosis, or diabetes in the family. The father is living and well; one sister died of cancer.

**Physical Examination.**—Temperature, 98.2° F.; pulse, 80; respiration, 16; weight, 145 pounds; height, 64 inches; an excess weight of 9 per cent., or 13 pounds.

She is well nourished, of good color, face a bit flushed, general attitude tense and hurried.

The teeth and gums are in good condition; several teeth have been lost. The tonsils are moderately enlarged, red, fissured, and exude caseous plugs on pressure. The edge of the anterior arches is reddened. There is no enlargement of the cervical glands; the thyroid is not visible or palpably enlarged.

The cardiac apex is in the fifth interspace midclavicular line; the left border runs just outside the left nipple and the right border just behind the right edge of the sternum. The aortic arch is somewhat broadened. There is a harsh *systolic murmur* at the apex which may be heard in the axilla; the second sound is accentuated, more so at the aortic cartilage than at the pulmonic.

The lungs are normal; the abdomen is normal, with the exception of fatness; vaginal and rectal examinations show no faults except a moderate relaxation of the perineum from laceration. There are no scars, edema, or abnormalities of the extremities. None of the superficial vessels show any hardening. Reflexes are normal.

The urine is acid, specific gravity 1.024, contains no albumin,

sugar, or casts. The phenolsulphonephthalein test shows 25 for the first hour and 35 for the second.

Blood: Hemoglobin, 100; red blood-cells, 4,920,000; white blood-cells, 5700.

Blood Wassermann is negative in all antigens.

Blood-pressure 170 to 120 at the first examination; later, when she was under less strain than at the first examination, it has been about 155 to 110.

The outstanding features in this case are considerable mental strain, fatigability, slight vertigo on change of position, a 9 per cent. excess of weight, infected tonsils, well compensated mitral regurgitation, and increased arterial tension. Of these the hypertension is the most important. There is no nephritis, arteriosclerosis, or other impairment to account for this.

You will note that the amount of urine passed in twenty-four hours is 1500 c.c.—the normal. No albumin or casts have been found on repeated examinations. The phenolsulphonephthalein excretion test shows a total of 60 per cent. in two hours. This is within the normal and shows a proper functioning of the kidneys as regards protein elimination. Moreover, she shows no edema of the extremities, which is an early sign of kidney insufficiency. The moderate dyspnea may be accounted for by her excess weight and endocarditis.

Arteriosclerosis is not demonstrable in the superficial vessels, but from clinical pathologic experience we would expect to find sooner or later the smaller vessels showing evidence of hardening. The case must then be considered as one of essential hypertension or hyperpiesis.

The question arises, What is normal blood-pressure? The profession has been much confused on this point, and we are frequently embarrassed to answer the question when put to us by patients. The old statement, that systolic pressure may be a figure equal to one's age plus a hundred, is *wrong* and one productive of harm. Such figures are entirely too high. Those given by J. W. Fisher (The Diagnostic Value of the Use of the Sphygmomanometer in Examinations for Life Insurance, issued by the Northwestern Mutual Life Insurance Co., De-

cember, 1922), in the examination of over 50,000 life insurance applicants, are more dependable and have come to be recognized as normals:

FISHER'S TABLE FOR NORMAL SYSTOLIC PRESSURE

Age periods.	Total cases.	Average.
15-19.....	880	120
20-24.....	3,920	122
25-29.....	5,892	123
30-34.....	6,343	124
35-39.....	7,146	126
40-44.....	13,849	128
45-49.....	9,537	130
50-54.....	5,294	132
55-59.....	2,379	134
60-64.....	680	135
65 and over.....	201	136

The average increase here is 0.34 mm. for each year of increase in age. Faught considers 120 mm. as the average for the age twenty and adds 0.5 mm. for each year. This gives rather higher figures than Fisher's table, but the two are near enough for either to be used as a guide. The normal systolic pressure varies and is particularly prone to be increased by nervous tension. Medical Officers in the World War, under the strain of examination for overseas service, frequently showed a pressure of 150 to 160 mm., when under better conditions the pressure would be 130 to 140 mm. Patients will often show a pressure considerably higher at the first reading than they will later when they are more composed. A pressure above 160 mm. has long been counted as pathologic, but this is probably 10 to 20 mm. too high; we would probably be safer were we to count 140 to 150 mm. as pathologic.

In a further study of 2610 accepted risks between forty and sixty years with an average systolic pressure of 142 mm. (normal 125-134) Fisher found the mortality was 14 per cent. above the normal expectancy. In 520 accepted risks of the same age period with an average pressure of 153 the mortality was 34 per cent. above the normal. He concludes "that a persistent systolic blood-pressure of about 12 mm. above the average

for the age would seem to indicate the limit of normal excess variation in man."

Janeway's figures on diastolic pressure have usually been accepted as a fair average. His table follows:

NORMAL DIASTOLIC PRESSURE IN 128 CASES

Age period.	Average.
10-13.....	80
20-29.....	85
30-39.....	85
40-49.....	85
50-59.....	90
60-69.....	90

It usually rises with systolic pressure, but not in the same proportion.

**Causes.**—The immediate cause of hypertension is probably a spasm of the smaller vessels. The increased resistance calls for increased pressure in order to maintain the circulation correctly. The causes of this spasm must be various. An important factor is *physical and mental strain*, and particularly the latter. This may be noted in routine blood-pressure examinations when the patient is excited. Persistent *overeating* appears in some cases to be a positive factor. Whether the surplus food causes the formation of toxic materials which, absorbed into the blood, act as stimulants to the vasoconstrictors and cause the spasm of the smaller vessels or not is a question remaining to be settled. It is significant, however, that persons with *intestinal stasis* frequently have increased pressure. Excessive use of *tobacco* appears to be a cause. It is still a debatable question how far *alcohol* may be considered as causing hypertension. The *menopause* has lately been thought a cause, and particularly when it is accompanied by obesity.

The altered functions of the *ductless glands* which accompany the menopause probably exert some influence upon blood-pressure. In some instances, however, this appears to be of little importance. The accompanying obesity may account for a small increase.

Essential hypertension is a disease of middle life, though it is occasionally met with in the young.

**Symptoms.**—Persistent increase in arterial tension may exist with no symptoms in the early stages. It may be discovered only in the course of a routine examination. *Fatigability* and *vertigo* are of the earliest symptoms; *lack of initiative* in mental and physical exertion are frequently noted. These symptoms seen in association with nervous instability may lead one to confuse the disorder with neurasthenia.

As the heart becomes involved *palpitation*, *irregularity*, and *dyspnea* may be seen as a consequence thereof. As the blood-vessels become hardened various symptoms develop, depending upon the location of the vessels involved. If of the abdomen, *distention* and other evidences of indigestion; if of the kidney, the symptoms of the contracted kidney—*edema* and *urinary changes*; if of the brain, symptoms of *hemorrhage*, *thrombosis*, etc. In advanced hypertension *headaches* may be persistent and severe. Janeway describes them as occurring early in the day and disappearing soon after breakfast or during the course of the morning. They have been called "lead cap headaches."

**Sequelæ.**—As has been stated, essential hypertension is a functional disorder and unaccompanied by pathologic changes. It is a warning of organic changes which will occur unless the conditions of life which produce it are altered.

The additional amount of work thrown upon the *heart* in overcoming the resistance of even a moderate increase in pressure soon causes hypertrophy and ultimately myocarditis.

Coincident with the myocardial changes are alterations in the *blood-vessels*. The constant strain upon them leads to sclerosis. The vessels of the viscera are among the first to be involved. The changes in the vessels of the heart, brain, and kidneys are of the most vital importance. The evil effect of such sclerosis are far reaching and most destructive.

With the occurrence of arteriosclerosis the *kidneys* become involved and the symptoms of the arteriosclerotic kidney appear. It is at this stage that these cases most frequently come under medical care. Previous to this time symptoms have been so slight that they have not called for relief. At this stage the pressure increases progressively and becomes less and less amenable to treatment.

**Treatment.**—In the treatment of this disorder it is essential that it be discovered early. As the symptoms are so slight it is seldom discovered except in routine examinations. This fact furnishes another reason for periodic health examinations. Further, we must revise the old ideas of normal pressure and accept the insurance companies' dictum that an increase of 12 mm. above the average seems to indicate the limit of normal excess. Elimination of nephritis and arteriosclerosis by methods at our disposal simplifies the problem by reducing it to one of essential hypertension.

Hypertension is compensatory in advanced cases with vascular and nephritic sequelæ and is so to a lesser extent in uncomplicated hypertension. Reduction measures must be entered into, then, guardedly and in association with removal of causes.

*Focal infections* must be persistently sought for and removed. In this patient the tonsils were infected and removed. A careful analysis of the patient's routine of life may reveal the faults which have a bearing on the condition. In this one the strain and worry of her work appeared to be causes. These have been removed so far as possible, but the effort she is making to keep her own house and work in an office makes a bad combination, productive of worry and hurry.

A period of complete *rest* in bed on a *milk diet* will effect a very good reduction. This improvement, however, is contingent upon mental rest in connection with the physical. If the patient worries and fusses, the rest will be of little value. If this period is followed by one away from business, the relief will be more permanent. This vacation will permit the sufferer to adjust himself to the condition and perhaps to see the futility of worry and tension and to appreciate the danger of the condition. The patient should have one or two periods of relaxation each day after resuming his work.

*Exercise* tends to increase pressure, but it is of so much value in promoting elimination and preserving a good metabolism that it should be indulged in to such an extent as the patient's condition permits or warrants. It should never be

hurried. Under such conditions the net result is a decrease in the pressure. Golf and walking are the best, for both tend to distract attention from the worries of business and domestic life.

*Foods* which disagree with the patient must be avoided. The effect of proteins upon blood-pressure is still undecided, but it is generally felt that abstinence from them is helpful. We do know that they are harmful in nephritis and it is believed by me that a large consumption of such is favorable to the production of nephritis. Therefore, it is well to limit them. A diet of milk, vegetables, and fruit is the best. Coffee and tea should be eliminated, for both increase pressure.

If habitual users of *alcohol* give it up, blood-pressure increases temporarily; this is soon followed by a gradual fall. *Constipation* must be avoided. Intestinal stasis has a bad effect on blood-pressure. Colonic irrigations are helpful. An occasional *mercurial purge* assists in elimination and is of advantage. *Tobacco* should be used sparingly or not at all. *Obesity* should be reduced moderately. Abstinence from alcohol and temperance in food will tend to reduce the overweight. Patients must not be so greatly reduced as to impair strength and vitality. When an individual suffering from hypertension begins to lose weight it is usually an indication of a grave prognosis.

*Pilocarpin hydrochlorate* in doses of 1/20 grain every three hours promotes diuresis; in larger doses up to 1/10 grain it causes free sweating or free secretion of the gastro-intestinal glands and the kidneys. In some cases it has been of marked value. The larger doses are prone to slow the pulse. The *bromid salts* serve a very useful purpose in controlling excitement and apprehension.

The foregoing treatment aims to reduce the pressure by removing the cause. In conjunction we are impelled to use, and often justifiably so, the vasodilators. Of these, *potassium* or *sodium nitrite*, in doses of  $\frac{1}{2}$  to 2 grains every three hours, and erythroltetranitrite, in doses of  $\frac{1}{2}$  to 2 grains every three hours, are the best. The action from these is more continued than from nitroglycerin and amyl nitrite, whose action begins quickly and has but a short duration.



## CLINIC OF DR. JOHN H. MUSSER, JR.

UNIVERSITY OF PENNSYLVANIA

### DIABETES AND TUBERCULOSIS

THIS combination of diseases is rather unusual, as tuberculosis is not more frequent in the diabetic than in the normal individual. Of course there are relatively few diabetics in the population, and the same may be said of those who have tuberculosis, so that to have the two coexisting calls for a selection by the two diseases from a relatively small group of people. Montgomery, in his studies of a large number of cases of tuberculosis, found that diabetes did not occur any more frequently in the tuberculous than in the normal individual. Such has been the statistical evidence of others. When diabetes does occur in the tuberculous we are face to face with a serious problem. Phthisiographers are pretty generally agreed that it is more important to treat the diabetes than it is to treat the tuberculosis. The accepted method of treatment until a few years ago was to attempt to build up the patient's tolerance by starvation, green days, and other time-honored methods for the treatment of the condition, and then, if these methods of treatment were successful, in overcoming the diabetic disturbance to attempt later on to force overalimentation of the patient. Landis and Funk,<sup>1</sup> among others, accentuate this point. The question has always been an extremely nice one and presents a real therapeutic problem. The patient should be so undernourished that his diabetes does not cause him to go into coma and death, and at the same time he should attempt to take the maximum amount of food in order to build up his resistance to the tuberculous process. Within the past year or two, however,

<sup>1</sup> Trans. Nat. Tub. Assoc., 1918, 14, 266.

with the introduction of insulin the former method of treatment of these coexisting diseases has been entirely changed. It is now possible with the aid of insulin sufficiently to nourish the patient so that he may gain weight and at the same time not have sugar in the urine, high blood-sugar, and so on.

The following is the history of a patient who was in the Presbyterian Hospital last summer, and whom I, together with other members of the dispensary staff, have had the opportunity of following during the past year. He has consented to come here today so that you may visualize how great has been his improvement.

**Case History.**—Mr. A., aged forty-two years, occupation is that of a foreman. He first commenced feeling sick February, 1923, when he noticed that he was becoming weak, had marked polyuria, intense thirst, and a voracious appetite, which symptoms have gradually increased in severity until the present time. For the last three months he has not worked and he has lost 50 pounds in weight. He has dieted very carefully, but has gotten gradually weaker. Says he is unable to do practically anything and he has the most intense thirst and hunger. He has no other symptoms apparently referable to other systems of the body. His past medical, family, and social history is unimportant. It is interesting to note that he knows of no one in his family who has had diabetes and there is no history of tuberculosis in the immediate family.

**Physical Examination.**—Patient is extremely emaciated, has a sweetish odor of acetone on his breath, slight edema of the ankles, and at the left apex there is detected an impairment of the percussion note, bronchovesicular breathing, and some exaggeration of fremitus.

**Subsequent Course.**—The diagnosis of tuberculosis was confirmed by the x-ray and by two positive sputa, as well as by the persistent temperature, which ranged as high as 102° F. in the afternoon. Four days after admission to the hospital, 60 units of insulin being given, Mr. A. became sugar free. The quantity of urine at the onset was between 3 and 5 liters a day. It rapidly fell until he was passing a small quantity of urine in

## WEIGHT AND BLOOD-SUGAR CHART

Date.	Weight, pounds.	Blood-sugar, mg. per 100 c.c.
7/ 9/23 .....	98	321
7/16/23 .....	102	200
7/18/23 .....	105 $\frac{1}{2}$	233
7/30/23 .....	112 $\frac{1}{2}$	200
7/31/23 .....	114 $\frac{1}{2}$	
8/ 6/23 .....	108 $\frac{1}{2}$	154
8/12/23 .....	108 $\frac{1}{2}$	181
8/16/23 .....	108	
9/10/23 .....	110 $\frac{3}{4}$	333
10/ 7/23 .....	117 $\frac{3}{4}$	170
11/ 5/23 .....	126 $\frac{1}{4}$	200
11/22/23 .....	130 $\frac{3}{4}$	143
12/17/23 .....	133 $\frac{3}{4}$	126
1/ 4/24 .....	132	267
2/ 9/24 .....	138 $\frac{1}{2}$	189
3/ 8/24 .....	141 $\frac{1}{2}$	222
4/ 5/24 .....	143 $\frac{3}{4}$	212
6/14/24 .....	146 $\frac{1}{2}$	Test unsatisfactory
7/19/24 .....	146 $\frac{1}{2}$	192

the twenty-four hours. He was given 60 units of insulin a day and in about ten days this was reduced to 45 units. His diet was gradually increased from 640 to 2500 calories, the proper ratio being preserved between the protein, fat, and carbohydrate, protein being a gram per kilo of body weight, and the fat ratio approximately equivalent to twice the amount of carbohydrates plus one-half the amount of protein in order to preserve the proper ketogenic-antiketogenic balance. The accompanying chart illustrates very well the improvement that has taken place in this man. He is only seen from time to time, but as he is an extremely intelligent individual and very much interested in his condition, the consequence is that he is permitted a great deal of leeway in the handling of his own case. He has become so well acquainted with carbohydrates, protein, fat, caloric values, and so on that he knows a good deal more than the average doctor about practical details. He has steadily examined his urine daily; if he finds there is any sugar he varies his dosage of insulin to a slight degree. Mr. A. started to work shortly after the first of the year and has been working steadily

ever since. Repeated examinations of his sputum have been negative. Physical signs in the chest have practically disappeared.

**Summary.**—This case presents a person with tuberculosis and diabetes which with the use of insulin and intelligent co-operation of the patient have both yielded successfully to treatment.

## SEVERE ACIDOSIS OF DIABETES

ONE of the most spectacular uses of insulin is in the treatment of diabetic coma. The results that are achieved at times are perfectly remarkable, and it is a tremendous amount of satisfaction to see a patient in coma or precoma who rapidly improves with the proper use of insulin.

Mrs. S., aged fifty-six years, was seen by me at her residence in typical coma. She was practically unconscious and could be roused only with great difficulty. She had a heavy odor of acetone on her breath and typical Kussmaul breathing. She was at once given 90 units of insulin hypodermically and was fed at the same time a home-made solution of sugar. In a comparatively few minutes she roused from her stupor, was able to answer with difficulty questions, but in a period of an hour she could talk sensibly and lucidly. She was at once admitted to the hospital and there she was found to have 360 mg. of sugar per 100 c.c. of blood. Her urine contained large quantities of diacetic acid and acetone as well as sugar. Her blood plasma  $\text{CO}_2$  was 39 volumes per cent. The patient was at once ordered 30 units of insulin every fourth hour, external heat, catheterized every twelve hours, and was given 20 grams of glucose by mouth every two hours. The following morning she was entirely conscious and was given a diet high in carbohydrates, containing protein grams 60, fat 43, carbohydrate 120. The accompanying chart shows the subsequent urinary and blood chemical reports of the case. Eight days later Mrs. S. was placed on a diet of 65 grams protein, 120 fat, 50 carbohydrate, total calories of 1540. Her convalescence was uninterrupted and she left the hospital in excellent condition.

Her subsequent history is particularly interesting. She was seen about three months later, and reported to me that she had kept on with her insulin daily. She was attended by her regular physician and had taken 25 units of insulin three times a day.

Date.	Amount.	Sugar, per cent.	Grams.	Acetone.	Diacetic.	Blood-sugar.
2/15.....	600	5	30	++	++	
	600	5	30	++	++	316
2/16.....	700	0.9	6.3	0	0	390
2/17.....	870	1.4	12	0	0	
2/18.....	710	+0.5	3.5	0	0	
2/19.....	850	0	0	0	0	286
2/20.....	300	0	0	0	0	
2/22.....	330	0	0	0		
2/23.....	1300	0.7	10.01	+	0	
2/25.....	1400	0	0	+	0	100
2/26.....	1380	0	0	+	0	
2/27.....	1475	0	0	+	0	
2/28.....	2280	0	0	+	0	
3/1.....	1515	0	0	0	0	
3/2.....	1800	0	0	0	0	200
3/3.....	1125	0	0	0	0	
3/4.....	1710	0	0	0	0	
3/5.....	1640	0	0	0	0	
3/6.....	1580	0	0	0	0	
3/7.....	1300	0	0	0	0	133
3/8.....	1410	0	0	0	0	
3/9.....	2020	0	0	0	0	

At no time had she any sugar in the urine. She was seen again about two months later. She was following a diet only comparatively rigorous, and she told me she had gotten tired of taking the insulin, had gradually cut down on the dosage, and, in fact, had given up the treatment almost entirely, due to the fact that her attending physician had said he thought there was not much use in taking the insulin.

Mrs. S. reported to me that she had no sugar in her urine for some weeks. This statement was confirmed by a twenty-four-hour specimen which I examined at the time and which contained no sugar. In spite of the fact that I urged her to continue with her treatment, she said she did not care to go on with it. Incidentally this is one of the problems that one has to meet in taking care of diabetic cases. The great majority of them freely and willingly adhere to the rules and regulations laid down by the physician, but to a certain percentage of the less strong willed the following out of the rigid rules becomes extremely irksome and they are quite willing to cease their treat-

ment upon slightest provocation or for no reason whatsoever except that they become tired of it, have difficulty giving themselves injections, and so on.

This patient's physician has reported to me once since then and told me she is still sugar free. The interesting events in this case are the very rapid recovery from the coma and the subsequent improvement brought about by the use of insulin, carbohydrate, and free intake of fluid. Also of interest is the fact that in spite of the discontinuation of the treatment she has remained sugar free. It is very hard to conceive of a patient in whom severe acidosis developed and who had practically no tolerance for sugar at the time of her admission to the hospital, in a comparatively few months recovering and to all intents and purposes being normal. Presumably this patient had an overwhelming exhaustion of the pancreas, and that as a result of the rest the insulin gave to the organ it came back to a more nearly normal status. It will be interesting to see her subsequent course.

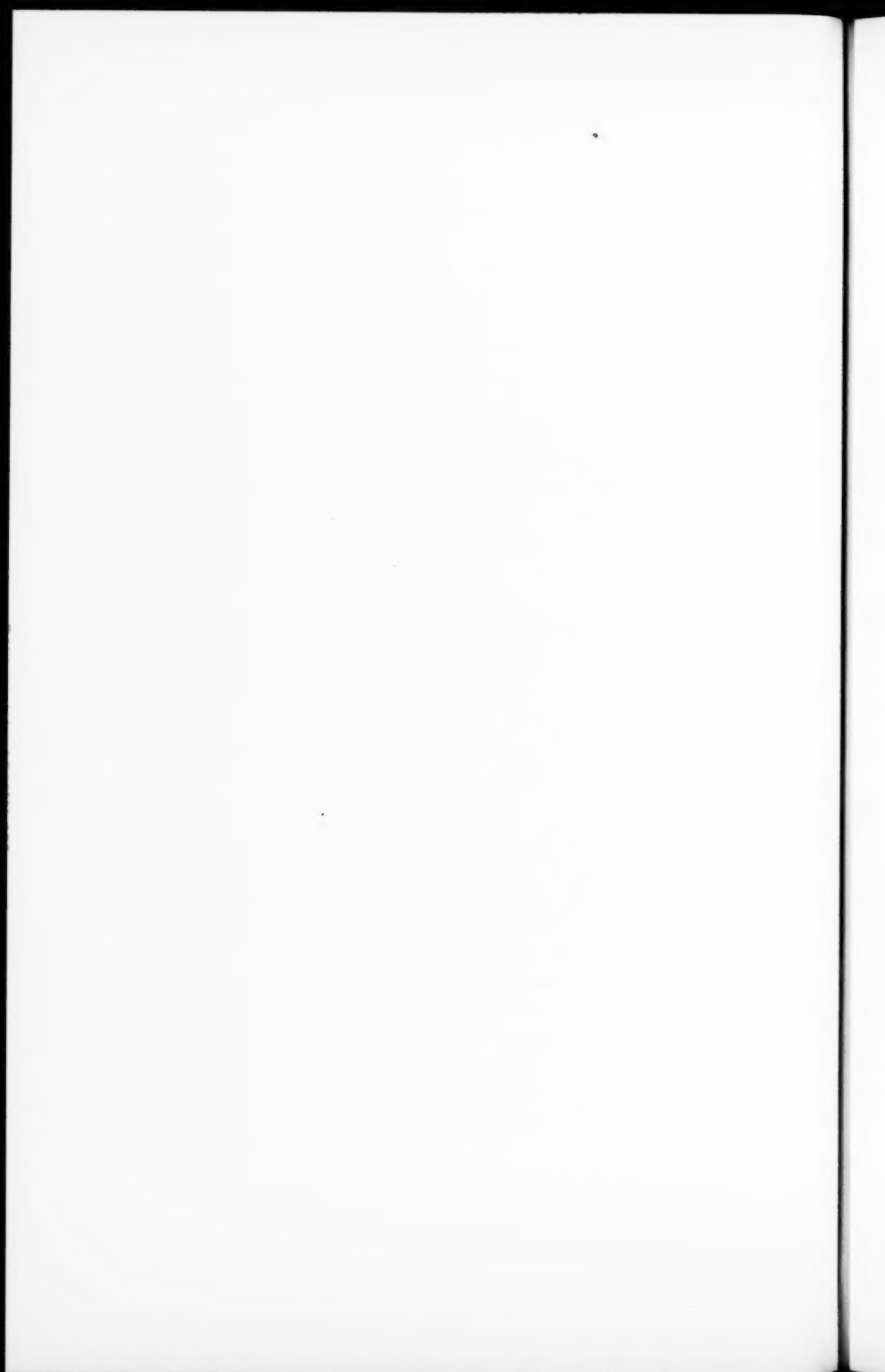
**Treatment of Coma.**—This brings up the question of the proper management and handling of a case of threatening or developed coma. Patients who are unable to afford proper nursing care at home should be removed to the hospital at once where they should be put in bed, kept warm, and kept as quiet as possible. The bowels should be kept moving daily by the use of enemata. Cathartics may cause diarrhea which is likely to increase the acidosis. If the pulse is weak, the patient has considerable shock, he should be given digitalis and caffeine. Liquids should be forced—1000 c.c. every six hours at least, preferably in the form of hot tea, coffee, or broth. If the patients are completely unconscious usually the preliminary dose of insulin will bring them out of their unconsciousness. They should be given 20 grams of glucose by mouth, which may be given in the form of cane-sugar or syrup. The first dose of insulin should be at least 50 units. If the person is absolutely comatose the insulin should be given intravenously in a 5 per cent. glucose solution. In the private home it is very difficult properly to prepare the glucose solution and usually it is enough to give 5 per cent. solution of glucose by bowel and the insulin hypodermically.

		Protein.	Fat.	Carbohydrate.
Breakfast:				
Grapefruit.....	150 gm.	0.6	....	5.7
Oatmeal.....	150 gm.	4.7	....	16.0
Egg.....	1	6.5	6.0	
Milk.....	50 c.c.	1.5	2.0	2.5
Tea or coffee.....				
Non-COH biscuit.....	2			
		13.3	8.0	24.2
Dinner:				
Broth.....	150 c.c.	3.5		
Meat.....	90 gm.	20.7	25.2	
Rice.....	100 gm.	2.8	....	24.0
Potatoes.....	100 gm.	2.0	....	20.0
Vegetables, 10 per cent.....	150 gm.	1.0	....	12.0
Milk.....	50 c.c.	1.5	2.0	2.5
Tea or coffee.....				
Non-COH biscuit.....	2			
		31.5	27.2	58.5
Breakfast:				
Orange.....	150 gm.	....	....	10.0
Oatmeal.....	200 gm.	6.5	....	22.0
Milk.....	50 c.c.	1.5	2.0	2.5
Coffee.....				
		8.0	2.0	34.5
10.30 A. M.:				
Oatmeal.....	200 gm.	6.5	....	22.0
Dinner:				
Broth.....	150 c.c.	3.5		
Potato.....	100 gm.	2.0	....	20.0
Rice.....	200 gm.	5.6	....	48.0
Milk.....	50 c.c.	1.5	2.0	2.5
Coffee.....				
		12.6	2.0	70.5
3.30 P. M.:				
Oatmeal.....	200 gm.	6.5	....	22.0
Supper:				
Oatmeal.....	200 gm.	6.5	....	22.0
Milk.....	50 c.c.	1.5	2.0	2.5
Coffee.....				
		8.0	2.0	24.5



Depending on the response of the patient the glucose should be forced or diminished, and the same may be said of the insulin. The wise rule is to continue giving the glucose 15 grams hourly and the insulin 10 to 40 units every third hour unless the sugar disappears from the urine. When these patients have become conscious, and they do become conscious in a very short time, they should be started on a diet high in carbohydrates in order to overcome the ketosis. Doctor Jonas and myself, in a description of a routine course in insulin therapy which we prepared last winter, suggest giving diets of a type as given on page 778.

As soon as the urine becomes free of diacetic acid the carbohydrate is reduced and the subsequent treatment is that of any case of diabetes.



## ALBINISM IN THE NEGRO

THE subject of albinism has for many years caused a great deal of discussion in medical literature, so much so that in looking over the references on the subject one finds that a large number of articles have been published. These were largely as isolated case reports until 1918, when an extensive monograph appeared on the subject from the Drapers Research Committee.

The question of albinism in the negro is one that has always raised considerable interest. The condition is rare, just how rare it is not known, as there are no definite statistical studies on this question. People who live in the South will tell you they may have seen 5 or 6 albino negroes in their life, but, of course, that indefinite statement is of no scientific worth. Doctor Heiser, among Filipinos, reports 45 cases in the population of the Philippines in the first decade of the present century.<sup>1</sup> Moore<sup>2</sup> reports a case of albinism in a negro and says that it is very rare, that he has only been able to find one reported case. A more extensive search of the bibliography will show that many more cases have been reported, and that not only in the American negro but also in the pigmented races of other countries the condition is relatively common.

It is well known that albinos exist in a relatively large number among certain species of animals—mice, rats, rabbits; whereas in cattle, horses, sheep complete albinism is rare though partial albinism occasionally occurs in these animals. It is quite generally agreed that among humans the condition is probably more frequent among the negro than among the white race.

Albinism is readily inherited. There can be no question but that in accordance with the mendelian theory albinism is a typically recessive characteristic. More albinos would appar-

<sup>1</sup> Philippine Journal of Science, 1913, 8, 493.

<sup>2</sup> Amer. Jour. of Dermatology and Genito-urinary Diseases, 1909, 13, 327.

ently be found were it not for the fact it is a usual rule that their physical health is poor and they die before they have the opportunity of propagation.

The **clinical characteristics** of a case of albinism are too well known to require description. A short description of the two patients who are illustrated here will suffice to describe all negroes who have albinism. The hair is wooly and kinky and a peculiar tawny whitish color. The face has a pinkish white color and the skin is dotted with small areas of pigment similar to freckles. The facial characteristics are those of the negro—

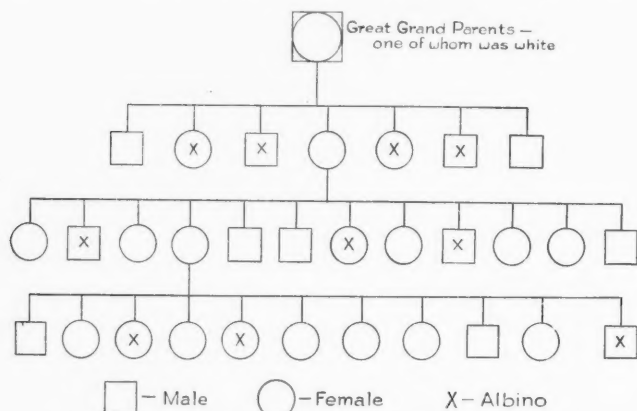


Fig. 135.—Family tree of three generations of albino negroes.

thick lips, flattened nose, and so on. These patients' eyes, as you see, are watery, they blink frequently, and give the evidence of intense photophobia. Both of these children have a well-marked nystagmus which is a frequent finding in a case of albinism, as is the photophobia. They are undernourished, mentally deficient, the girl child of seventeen having as yet not passed the second grade, part of this may be due to the weak eyes, which have never been attended to. Nystagmus is not a *sine qua non* for the diagnosis of albinism, but is an important supplementary finding, as is photophobia. Likewise the tendency to mental

deficiency, to menstruation late in life in women, and to generally poor health in both sexes are characteristic of the disorder.

I have been able to go back three generations in this patient's family tree. Short duration of life is the rule in such a family. You find that the mother of these 2 children has had 11 children, only 3 of whom are alive at the present time. She, in turn, had 11 brothers and sisters, of whom only 3 obtained maturity.



Fig. 136.—Two negro albino children.

And of the 11 direct descendants on the mother's side of the family, only 4 of them reached the age of maturity. Of the 3 children who were albinos, 1 lived to be three or four years of age. One of the albinos in the aunt and uncle's family lived to maturity and 2 in the great aunt's. One of the great grandparents was supposed to be white and the mother certainly shows evidence of having white blood, although this probably has no effect whatsoever on the albinism itself. The family tree,

I think, is accurate. The albinos with which the mother was acquainted all seemed to have nystagmus, and she says that in all of them did the "eyes dance."

**Summary.**—Albinism is a congenital lack of pigment occurring more frequently in some species than others and apparently common in the negro race. To what this lack of pigment is due is not known, but it may possibly be a metabolic disturbance, as suggested by Niles, in which the pigment of the body is not so prepared that it may be utilized in the skin and the eye.

Two cases of albinism are shown together with a family tree of three generations.

## CLINIC OF DR. CHARLES C. WOLFERTH

UNIVERSITY HOSPITAL

### INANITION EDEMA ASSOCIATED WITH ALIMENTARY DISTURBANCES IN ADULTS

I WISH to present 2 patients today both of whom have developed generalized edema following profound alimentary disturbances. This type of edema is doubtless closely akin to if not identical in nature with the war edema which was so common in certain European countries in the later stages of the recent war. It is probably more frequent as a manifestation of inanition in ordinary peace-time practice than is generally recognized.

The condition has been described under a variety of names, among which the best known are war edema, famine edema, prison dropsy, nutritional edema, and inanition edema. Of these, inanition edema is probably the best name, since the most important factor in the causation of the edema is properly emphasized.

Although little attention was paid to inanition edema prior to the recent war, the condition has been known for many centuries. A number of outbreaks were recorded during the Middle Ages and one in France as early as the sixth century. Probably the earliest case in the literature is that of the philosopher, Heraclitus, who lived about 2300 years ago. Lusk, in his recent review dealing with the physiology of undernutrition (*Physiological Reviews*, vol. 1, 1921), quotes Diogenes Laertius as saying that Heraclitus, despairing of mankind (a view, as you see, far in advance of his time), retired to the mountains, where he lived entirely upon vegetables and herbs, became dropsical, and died. Thus inanition edema has an ancient if somewhat

obscure position in nosography, and in spite of the recent rather voluminous European literature, is scarcely to be regarded as a parvenu.

Inanition edema is easy to diagnose and also easy to treat except where treatment is rendered ineffective by some underlying disease. Failure to recognize it in well-developed cases is due to ignorance of the condition, failure to think of it or carelessness in the study of a patient. Yet, prior to admission here, the first patient I will show you had been diagnosed nephritis, and the second was suspected of having both cardiac and renal disease.

Our first patient, G. L. B., a white American, fifty years old, had a highly acute attack of appendicitis in 1920. He was promptly operated on in this hospital, when a perforated appendix and diffuse peritonitis with a great deal of free pus in the peritoneal cavity were found. Following operation he was desperately ill for a number of days, but then slowly began to improve. A fecal fistula developed which did not heal for four months. A great deal of the anterior abdominal wall was destroyed by infection. After healing of the wound he was left with the tremendous abdominal scar, which, as you can see, is almost round in shape. It measures roughly 12.5 by 14 cm. It is very thin walled and the intestinal peristalsis is easily made out under it. The rectus muscles in this area are apparently completely destroyed. Note also the scar of a counterdrain in the right flank. We must be convinced that tremendous abdominal infection was present and that our patient was fortunate to escape with his life.

Following recovery from operation he returned to his work as a clerk and was practically well for three years except for the necessity of constantly wearing an abdominal support. About nine months ago he began having several bowel movements daily. He states that the stools were bulky, gray in color, and had a very foul odor. He slowly began to lose weight and grow weaker, but was able to continue his work until four months ago. Recently he has become very much weaker, so that now he is



scarcely able to walk. In spite of his obvious edema he has lost about 35 pounds in weight, indicating an even greater loss of flesh. The appetite is poor and he is annoyed by gaseous distention. The frequent large stools have persisted in spite of dietary and medicinal treatment. He has gradually been growing more nervous during the last nine months. Recently he has been somewhat short of breath, but by no means orthopneic. About two weeks before admission swelling of the eyelids and ankles was first noted. Albumin is said to have been found in the urine and a diagnosis of nephritis was made.

The medical history prior to the attack of appendicitis in 1920 is negative except for a carbuncle eight years ago and an attack of pleurisy twenty years ago. He has done clerical work all his life. There is nothing bearing on the present illness in either the social or family history.

Examination on admission showed marked emaciation and pallor of the skin and mucous membranes. There was generalized edema involving the face, forearms and hands, lower part of the back, legs and feet, scrotum, and prepuce. There were signs of a moderate amount of fluid in the right chest and the abdomen. The heart was not enlarged and there were no murmurs, but the first sound was of poor quality. The radial pulse was small and soft and the blood-pressure 90/60. There were no evidences of peripheral arteriosclerosis. The eye-grounds were entirely normal in appearance. Examination of the lungs was negative except for the signs of fluid at the right base and a few sonorous râles at both bases. The abdomen was distended due to the presence of gas and fluid. The liver did not extend below the costal margin and the spleen and kidneys were not palpable.

The urine was persistently of low specific gravity, varying from 1003 to 1014. Some specimens showed no albumin, others very slight traces. In 5 microscopic examinations no casts were discovered; in 2, a few hyaline casts. Traces of sugar were found twice. The blood urea nitrogen was 21 mg. per 100 c.c., and the phthalein excretion 50 per cent. in two hours. Several blood-counts showed the cellular constituents to be normal and

the hemoglobin content was over 95 per cent. The fasting blood-sugar was 0.094 per cent. The blood Wassermann was negative. The blood-serum protein content was 3.3 per cent. (normal 7.7 to 8.8 per cent.), of which 10 per cent. was estimated to be serum globulin and 90 per cent. serum albumin. The conductivity of the serum (corrected for the low protein content) indicated that the concentration of inorganic salts was about the lower normal level (0.755). The cell volume of the blood was 44.8 per cent., thus affording confirmatory evidence of the absence of anemia. The basal metabolic rate was 20 per cent. below the normal. In the study of the gastro-intestinal tract the following results were obtained. The gastric content showed low acidity, the highest figure of free HCl reached in fractional study being 10. Duodenal content gave normal reactions for amylase and lipase, but on two occasions the laboratory reported that they were unable to obtain evidence of tryptic activity. The feces were bulky, there being two to four large movements every day. They were brownish gray in color and were laden with fat and undigested vegetable matter. In spite of the reported absence of trypsin in the duodenal content, the feces have not averaged over 2 grams of nitrogen per day. Carmin passed through the tract in eight hours and on a second trial in nine hours. *x*-Ray study following a barium meal showed no disease of the stomach or duodenum. The opaque substance was completely evacuated in eighteen hours.

Our patient has now been in the hospital five weeks and during this time we have tried in various ways to feed him a high caloric, high protein, easily assimilable diet. This has not been very successful, partly because aversion to food made it difficult for him to take much (although he did average about 2000 calories a day), and partly because of poor digestion and rapid passage of food materials through the gastro-intestinal tract which interfered seriously with absorption. During the first four days of treatment the edema lessened appreciably and the weight dropped 6 pounds, but since then it has remained about stationary. In spite of all our attempts at treatment, the character of the stools has not changed, although they are somewhat

less in amount and fat content. There has been no appreciable change in strength and general nutrition. The circulatory findings have remained about the same and the blood-pressure has averaged about 80/50. There has been a more or less constant tendency to slight tachycardia, but no fever at any time.

The case just presented is of clinical interest from several points of view, but we shall have to limit our discussion to a consideration of the edema. Although the distribution of the edema is similar to that of renal origin, the urinary findings and studies of kidney function at once compel us to admit that if this is renal edema, it is not one of the varieties we are accustomed to see. Let us therefore put on the blackboard the causes of generalized or universal edema that might conceivably come under consideration here and discuss our case in relation to them.

**Clinical Causes of Generalized Edema.**—1. Heart failure of congestive type.

2. Kidney diseases (acute nephritis, subacute and chronic tubular nephritis including mixed types of nephritis with tubular involvement, nephrosis).

3. Diabetes mellitus (undernutrition, administration of large amounts of soda, insulin, or a combination of these).

4. Advanced anemias and cachectic states, especially pernicious anemia and leukemia.

5. Late or terminal stages of chronic infections.

6. Deficiency of vitamins (beriberi and scurvy).

7. Allergic manifestations.

8. Drugs and poisons (particularly iodids, arsenic, snake venoms).

9. Inanition.

When we come to consider whether the edema found in our patient may be accounted for by any of the causes listed, we can immediately strike out from consideration groups 3, 4, 5, 6, 7, and 8. Although traces of sugar were twice found in the urine the presence of diabetes of a grade of severity sufficient to cause edema is out of the question. The blood-sugar was entirely normal and there were no symptoms that might be re-

garded as of diabetic origin except the loss of flesh. Advanced anemia and other blood diseases that might cause edema are ruled out by the blood studies. Our patient at no time during his present illness has shown any evidences of an infection. Beriberi is easily excluded by the negative neurologic examination including the absence of reactions of degeneration in the muscles. There are no clinical evidences of scurvy, nor has the diet been of a type that might permit the occurrence of scurvy. Swelling of allergic origin or that due to drugs or poisons is out of the question.

Features in the clinical picture that might suggest heart disease are the extremely low blood-pressure, the small soft pulse, and the weak first heart sound. The significance of these in our patient will be discussed later. The circulation is undoubtedly sluggish and this may have been a factor in the aggravation of the edema, but heart disease may not properly be regarded as a cause of the edema. There is no evidence of structural heart disease, no serious disturbance of respiration, and no cyanosis, phenomena that might be expected to accompany such an extensive edema of cardiac origin. Furthermore, the distribution of the edema, particularly the swelling of the face, the lack of moist râles in the lungs, the lack of engorgement of the veins or enlargement of the liver, easily exclude a cardiac edema.

Although the distribution of the edema is similar to that of renal origin, the forms of kidney disease causing dropsy are almost invariably accompanied by large amounts of albumin and numerous casts in the urine. There is one apparent exception to this statement—chronic glomerular nephritis—but this is no true exception since the edema found in this condition is circulatory rather than renal in origin unless the nephritis is diffuse and involves the tubules. In our patient not only was the urine remarkably clear of albumin and casts (particularly in view of such extensive edema), but, in addition, the low normal salt content of the blood, the capacity of excreting as much as 2 liters of urine a day, the normal phthalein output, and the normal blood urea nitrogen appear to indicate practically nor-

mal renal function. On these grounds all who have studied the patient in the ward are agreed that edema of renal origin may be excluded.

The discussion has now led us to the consideration of inanition edema. What are the characteristics of inanition edema? It is a condition occurring usually during war famine or pestilence, that is to say, at times when food is very scarce and extremely difficult for certain classes of the population to obtain. The outstanding features are loss of flesh, weakness, and edema. The loss of flesh is at first almost entirely at the expense of body fat; in extreme cases it had been found that the fat had almost entirely disappeared. When the store of fat grows low, the consumption of protein tissue becomes active so that marked atrophy of muscles and even of parenchymatous organs occurs. It is also of interest that some studies of necropsy material has shown complete disappearance of glycogen from the liver and muscle fibers. It is not surprising, therefore, that one of the outstanding clinical features is muscular weakness. In contrast to beriberi, however, there are no disturbances in either motor or sensory apparatus. Animal studies by McCarrison show that inanition causes atrophy of the thyroid, pancreas, and gonads, but enlargement of the adrenals and increased content of adrenalin.

In cases with the mildest grades of edema there may be only slight swelling over the dorsal aspects of the feet and the ankles. Swelling of the face usually occurs fairly early. The edema may become very extensive with large accumulations in the pleural spaces, peritoneum, and scrotum. In connection with the edema many observers have called attention to the pallor which may be present even without reduction in hemoglobin percentage.

The cardiovascular symptoms are of unusual interest. Most authorities have laid stress on bradycardia which is often a conspicuous feature. Pulse-rates as low as 36 to 42 are said not to be rare (Jansen). The heart sounds are usually weaker than normal and the blood-pressure decidedly low. The pulse is soft and of small volume. Coldness of the extremities is frequently complained of.

Another symptom that has been emphasized is polyuria. It is by no means certain, however, that polyuria is necessarily a symptom of inanition edema. It may have been due, in the war cases, to the highly liquid character of the diet, so much of which was made up of thin soups and vegetables of high water content.

The temperature is usually subnormal. Fever, according to one of the authorities on this subject, may be regarded as evidence of one of the intercurrent infections which these unfortunates so easily contract.

There are a number of deviations from the normal among the clinical laboratory findings. Usually there is a mild or moderate anemia with a normal color index and a tendency to leukopenia, but in some cases the blood-count and hemoglobin content are quite normal. The inorganic salt content of the blood-serum is normal or slightly below normal. The waste nitrogen substances are not retained above the normal levels. The most striking feature is the diminution of serum protein which is usually quite marked. The normal serum albumin-serum globulin ratio is maintained in contrast to what occurs in the so-called nephrosis in which it is reversed. The level of blood-sugar is normal or reduced. According to some authors there is a loss of calcium and the blood calcium content is below normal. The basal metabolic rate is usually decreased, but in advanced stages may actually be increased.

In the discussions as to the cause of inanition edema a number of possible factors have come under consideration. It could hardly be otherwise in view of our deficient knowledge concerning the pathogenesis of edema. Those which have received most notice are: (1) deficiency in quantity or quality of food, (2) abnormalities of intake, output or balance of inorganic salts and water, and (3) injuries to the tissues, particularly the capillary endothelium affecting their permeability.

Undoubtedly the most important factor is insufficient nutriment for the requirements of the individual. There have been numerous inquiries as to whether this lack is qualitative (lack of some particular element of food) or quantitative (in-

sufficient amount of food). We know that each person needs, in addition to the requisite fuel value of food, vitamins, certain inorganic salts, water, and an irreducible minimum of protein. It has been shown in some carefully studied cases of war edema that mere increase of the fuel value of the diet abolished the edema. This could be done by adding either fat or carbohydrate to the basic diet. In either event the result was the same, and not only did the patients lose their edema, but showed marked general improvement. Moreover, nitrogen output diminished, indicating that protein metabolism was spared by adequate diet, no matter whether predominantly fat or carbohydrate. There is some evidence, however, that the minimum protein requirement in inanition is greater than in the well nourished.

Another observation that appears to emphasize the disparity between caloric requirement and supply as an important factor in the production of edema, is the fact that many persons in the war-stricken countries receiving a strictly limited diet and doing heavy physical labor became edematous, but when put at rest, although still receiving the same diet, got rid of their edema. Thus a diet adequate to sustain nutrition with the subject at rest may not be sufficient to prevent the occurrence of inanition edema following physical exertion.

Some writers have been of the opinion that disturbances in the calcium and sodium chlorid balances are also of importance in the production of inanition edema. During the last few years the belief that calcium has an important rôle in helping to regulate the water currents of the body has assumed more and more prominence. The exact mechanism of its action is not clearly understood, but it is believed by some to "tighten" semipermeable membranes, particularly capillary endothelium, and thus retard the interchange of water and salts. Low calcium content of the blood such as claimed to be present in inanition edema is said to permit the capillary endothelium to be more permeable than usual and so favor the production of edema. Although the attempt has been made to connect sodium chlorid retention with the occurrence of edema, as has been done in nephritis, the evi-

dence at hand does not seem to favor this view. In nephritis there may be impairment of ability to excrete salt so that it tends to be stored up in the body. Under such circumstances it may be drawn to the tissues and play a part in diverting water currents so as to cause edema. In the case of inanition edema there is usually no impairment in the ability of the kidneys to excrete salt, and the blood content and the edema fluid content do not tend to be elevated. While it is true that the diet of war edema cases has usually contained large amounts of salt, excretion has been correspondingly large and experiments of feeding additional salt have shown no more than temporary delay in excretion.

It has been shown in war edema cases that additional amounts of water in the daily intake were promptly excreted, and there is no evidence that difficulty in excreting water is a factor of any importance in the production of the edema. On the other hand, it is quite probable that limited water intake may operate to prevent the occurrence of edema. It is a common experience to see cases of carcinoma of the esophagus or stomach with profound inanition, and instead of edema a state of extreme dehydration.

In recapitulation, we may say that quantitative insufficiency of nutriment furnished the body tissues has been demonstrated to be an important factor in the production of what is called inanition edema. That qualitative deficiency of either protein, fat, or carbohydrate, deficiency or retention of inorganic salts, or excess of water intake, play any part, has not been proved, although in the present state of our knowledge they cannot be ruled out. Deficiency of water intake may prevent the development of edema in cases that otherwise might be expected to become edematous.

When we come to compare the findings in our case with those of war edema certain differences are to be noted. The inanition has been caused not by insufficient intake of food, but by insufficient absorption. Whether this is due to pancreatic insufficiency or to some severe intestinal disturbance, either of which may be an end-result of the tremendous abdominal infection



three years ago, need not concern us here. The points of importance are that ingested matter moves rapidly through the gastro-intestinal tract and that the feces contain large quantities of fat and other undigested material. In addition to this, the patient's appetite is poor, so that he is unable to take much food. Comparison of the nitrogen content of his food intake with nitrogen studies of the urine and feces show that abundant nitrogen is being utilized to take care of his protein requirements. The total caloric value of the food assimilated is, however, undoubtedly insufficient for his needs.

The marked emaciation, the muscular weakness, the low blood-pressure, and the distribution of the edema all correspond to the clinical picture found in war edema. Bradycardia is lacking; on the other hand, there has been a tendency toward tachycardia, the pulse-rate ranging between 100 and 120. The urine output has not exceeded 2 liters a day and sometimes has been very much less, but this is probably due to the lower fluid intake in our patient than that of the war edema cases.

Among the clinical laboratory tests we find a close resemblance to those of war edema. The urine almost entirely clear of albumin and casts, the tendency toward low specific gravity, the normal kidney function tests, the low normal conductivity of the blood-serum, and especially the low serum protein content with preservation of the normal serum albumin-serum globulin ratio, and the low basal metabolic rate are all in accord.

On the basis of the facts presented I think that there can be no doubt that we are dealing with inanition edema. There are certain points of clinical importance whose discussion I should like to defer until after the presentation of our second case.

S. W. is a Russian Jew, fifty-six years old. He states that he was perfectly well until he had an attack of acute appendicitis five months ago for which he was promptly taken to a hospital and operated on. Drainage was required, but the wound closed after thirteen weeks and he was permitted to leave the hospital. A few days later an opening appeared in the wound and fecal

material and particles of food that had been eaten were discharged. During the next few weeks, up to the time of his admission here, there were alternating periods of a few days each during which the tract discharged freely or was almost entirely closed. While the tract was practically closed there was a great deal of vomiting, abdominal distention, and discomfort. As soon as it began to drain again, he would feel very much better and the distention would lessen, but not entirely disappear. He was markedly constipated. He stated that he had lost 47 pounds since the beginning of his illness.

The past medical history, social history, and family history are all unessential.

On admission he was found to be emaciated and so weak that he could scarcely walk. There was marked pallor of the skin and mucous membranes. There was some edema of the face, particularly the infra-orbital pouches. There was soft edema of the forearms and hands and the legs below the knees. The dorsal surfaces of the hands, the ankles, and feet pitted deeply on pressure. There was no evidence of fluid in the chest or abdomen. The lungs were somewhat emphysematous, but otherwise negative. The heart was normal in size, the sounds were of good quality, and there were no murmurs. An occasional premature beat was heard. The pulse was of poor quality and the blood-pressure 90/54. The peripheral arteries were somewhat thickened and Dr. Baer reported angiosclerosis in the eye-grounds. There was moderate gaseous distention of the abdomen and a fistulous opening, which, as you can see, is still present in the operative scar, discharging fecal matter.

The urine has been examined many times. The specific gravity has varied from 1010 to 1022. There has never been more than a trace of albumin and a few hyaline casts. Otherwise the urine has shown nothing of importance. The phtalein excretion after intramuscular injection was 50 per cent. in two hours. The blood-urea nitrogen was 15 mg. per 100 c.c. The erythrocyte count has always been over 4,500,000 and the hemoglobin over 90 per cent. At times there has been a slight leukocytosis and at other times the count has been normal. The

Wassermann test was negative. The serum protein was 4.6 per cent. (normal 7.7-8.8 per cent.), of which 70 per cent. was serum albumin and 30 per cent. serum globulin. The sodium chlorid equivalent of conductivity of the blood-serum (corrected for the low protein content) was a low normal (0.761).

Treatment was restricted to dietary measures and daily colonic irrigations. The principles of diet sought were high caloric value, abundant protein, easily assimilable foods leaving small residue. Fluid was limited to 1500 c.c. daily. No attempt was made to restrict salt intake.

During the three weeks the patient has been in the hospital he has shown remarkable improvement, although his co-operation cannot be described more charitably than to call it fair. Nevertheless the nurses have managed to get him to eat fairly well. As you can see, one may no longer properly call him emaciated, his color while not exactly rosy is certainly not pallid, and there is no edema demonstrable except very slight pitting over the tibiae and the dorsal aspects of the feet. The blood-pressure has risen to 120/80 and he is much stronger and more active. We now plan to refer him back to the surgeons for the relief of partial obstruction of the bowel and closure of the fistula.

Our second patient has many obvious points of resemblance to the first. Here is a man who states that he was perfectly well until his attack of appendicitis and operation several months ago. Since that time not only has he had a poor appetite and vomited a great deal of what he ate, but for a number of weeks part of what was eaten was rapidly lost through the fistula. Again, we have a patient with grave interference with gastrointestinal function. He, like our first patient, lost a great deal of flesh and showed marked wasting of muscles. There was a similar type of distribution of the edema, although it was much less in amount, and there was pallor in the presence of a practically normal blood-count. The blood-pressure was also decidedly low. There were striking similarities in the clinical laboratory tests including the low serum protein content.

The diagnosis of inanition edema may be established as easily in this patient as in the one you saw first. Furthermore, we have added confirmation of the diagnosis, since it has been possible to almost entirely abolish the edema and improve the general condition tremendously merely by increasing the assimilation of nutriment.

There is one fundamental difference between war edema and edema due to inanition encountered in civil practice where food is plentiful. In the latter there is to be found almost certainly some underlying pathologic process interfering with nutrition, and this may be expected to modify the clinical picture. Yet the condition is a clear-cut entity not difficult to recognize when its possibility as a cause of edema is considered.

There are certain points of clinical interest that deserve mention. I have emphasized the pallor of both these patients, yet both had a normal blood-count. I am unable to explain satisfactorily the reason for this pallor. The small soft pulse would seem to indicate a subnormal blood flow through the tissues. Furthermore, a waterlogged condition of superficial tissues would tend to make for an appearance of pallor. You may have noticed similar high grade of pallor without anemia in a case of nephrosis with edema recently in the wards. Several blood-counts were necessary in that case before everyone was convinced that no anemia was present.

Another point worth noting is the fact that not only had practically all the superficial fat vanished in both these cases, but there was very evident marked atrophy of muscles as well. We should remember that while fat suffers the greatest loss, protein tissues, including parenchymatous organs, are not spared in high grades of inanition.

We are at a loss to explain the striking and characteristic circulatory phenomena. It is well known that circulatory "adynamia" and very low blood-pressure may occur in association with advanced undernutrition without edema; we have had a number of such cases in the wards. Undoubtedly the heart is implicated in this process, but in just what way is not clear. We may speculate on the importance of atrophy of the muscle

fibers, deficiency in glycogen content, or some other nutritional disturbance. The basal metabolism is low. Is the sluggishness of heart action due to underactivity of an atrophied thyroid gland? In spite of the fact that McCarrison has found in experimentally produced inanition enlargement of the adrenals with increased adrenalin content, may not these glands actually function below normal and thus produce effects on the circulation in inanition similar to those they are supposed to cause in Addison's disease? These are questions that cannot be answered at present.

Although it has been pointed out that quantitative insufficiency of nutriment is of great importance in the causation of edema, little is known as to the actual mechanism of its production. We know how efficiently the normal composition of the blood is maintained in health. Why does the blood become hydremic, losing part of its protein content in inanition edema? Possibly for the same reason that parenchymatous organs lose protein. We do not know. The profound changes in the composition of the blood-serum suggest that there may be similarly profound changes in the cellular tissues. Possibly the edema is a process tending to help bring about a state of equilibrium between the blood and tissues and may, therefore, be of the nature of a compensatory process. At any rate, the details, for the present, remain obscure.

Krogh, in his recent remarkable book *The Anatomy and Physiology of Capillaries*, the careful study of which will more than repay you, states that "the exudation and eventful reabsorption of fluid in the intercellular spaces will depend upon the capillary blood-pressure, the colloid osmotic pressure of the blood, the permeability of the capillary wall, the efficiency of the lymph flow, and the metabolic activity of the tissue cells. It cannot be surprising that the process resulting from the interaction of these factors is often difficult and sometimes impossible to disentangle."

Concerning the capillary blood-pressure, the permeability of the capillary wall, and the efficiency of the lymph flow in inanition edema we know nothing. We assume that the metabolic

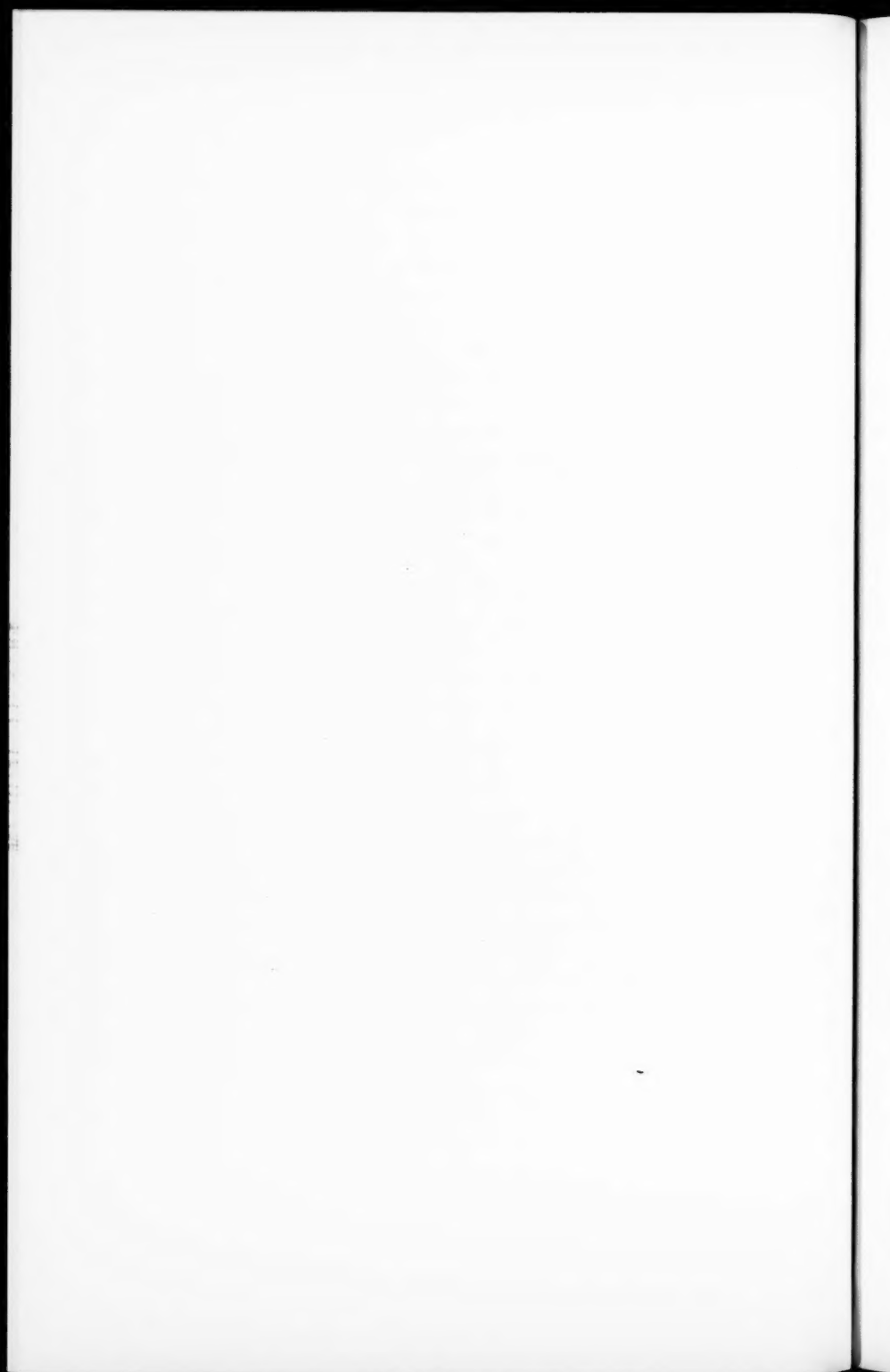
activity of the tissue cells is depressed since the metabolic rate of the body, taken as a whole, is below normal. We do know, however, in the 2 cases shown today that the colloid osmotic pressure of the blood is tremendously lowered since this depends on the serum protein content. Under such circumstances the blood is less able to take up fluid from the interstitial spaces and the formation of edema is therefore favored. The view that alterations of capillary permeability produced by calcium loss from the body play a part in the production of inanition edema, offers an attractive speculation, but in the present state of our knowledge no more than a speculation.

There is probably no condition easier to treat, if sufficient food is available, than mild uncomplicated inanition edema. In severe prolonged cases the mortality is by no means negligible, partly due to the ease with which the victims are attacked by intercurrent infections and their lack of resistance to these infections. While it is quite probable that irreparable damage to organs may result from inanition, it is remarkable how quickly and satisfactorily recovery can take place. If sufficient food can be utilized, it apparently makes little difference whether protein intake is high or low, provided only that the minimum protein requirements are satisfied, nor whether the bulk of the diet is made up of fat or carbohydrate. Treatment according to Jansen consists mainly of the effort to overcome the deficiency of caloric value of nutriment supplied with respect to that demanded. Bodily rest is particularly important since exertion increases food requirements. Lusk states that during the food scarcity in Germany a well-known mathematician did his work in bed.

The so-called cardiac stimulants and diuretics are useless. Apparently nothing is to be gained by drastic restrictions of salt and water intake. Calcium is recommended by some investigators as effective in aiding the discharge of the edema fluid. The use of thyroid extract is also said to favor the discharge of fluid, but this form of treatment may be a two-edged sword and cut both ways. We do not know whether the lowered metabolic rate is due primarily to lessened activity of the thy-

roid gland or is a compensatory mechanism of the body to resist inanition, but no matter which, the lowered rate would appear to be providential in helping to conserve the body tissues. This is more important than the mere discharge of fluid. The advantage of feeding thyroid requires convincing demonstration before this treatment is to be recommended.

In the cases of inanition edema encountered in peace-time practice, the treatment and also the prognosis must depend on the underlying condition responsible for the inanition. So far as the edema is concerned, if we are able to make the patients assimilate sufficient food, we may expect decrease of the edema as one of the first symptoms of improvement.





## CLINIC OF DR. B. B. VINCENT LYON

JEFFERSON HOSPITAL

### THE VALUE OF NON-SURGICAL DRAINAGE OF THE BILIARY TRACT AS A THERAPEUTIC MEASURE

I HAVE to show you today 5 cases each one of which presents special points of interest from gastro-intestinal as well as general clinical viewpoints. These cases have a larger importance because they have been followed up carefully for several years, and end-results are given.

The first case illustrates the restoration of gastric, gall-bladder, and intestinal function after appendectomy and post-operative "follow-up" management.

**Case I.**—Five years ago a young woman of twenty-eight complained of recurrent attacks of acute enteritis accompanied by nausea and vomiting, and paroxysmal abdominal cramps. The stools were green, of a foul odor, and with increased mucus. Seven years earlier the first attack occurred, with an interval then of six and a half years, but during the succeeding six months she had five distinctly acute attacks. All of these just preceded or followed menstruation, but this seemed to be purely coincidence, for there were no features in the attacks suggesting pelvic disease. All of the attacks were accompanied by nausea and retention vomiting, her stomach becoming quite rigid with diffuse, but exquisite sensitiveness. (Her husband, a doctor, vouches for this.) The attacks were followed by localizing residual soreness in the right iliac fossa, lasting for several days, immediately after which this patient felt perfectly well, except for what she called "periods of biliousness."

When sixteen years old she had had a severe attack of whoop-

ing-cough with violent paroxysmal coughing and vomiting, with pronounced retching. Otherwise her history was negative, beyond the fact that she had been married eight years without conception.

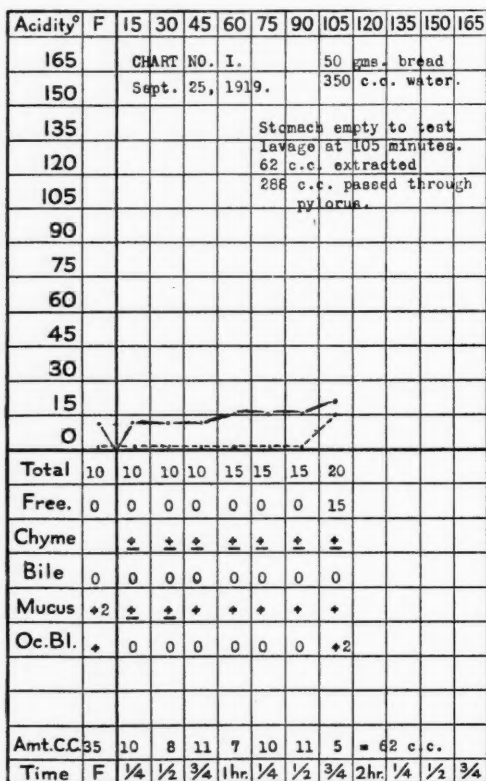


Fig. 137.

Her physical, including pelvic, examination between attacks was negative. She was a well-developed and nourished young woman, who gave every appearance of good health.

On September 25, 1919 her gastric analysis showed a partial

chemical achylia (sometimes called delayed digestion) up to one hundred and five minutes, when 15 degrees of free acidity occurred in the last extraction (Chart I, Fig. 137). Enzymes negative, but proenzymes present. This gave a favorable prognosis for restoration of gastric secretory function inasmuch as it suggested that there was not total destruction of secreting glands as in a progressive atrophic gastritis. There was greatly increased tenacious mucus of gastromyxorrhic type. Occult blood in faint traces throughout. Lactic acid present. Wolff-Junghans test: 1/40 (benign ratio).

Her biliary tract drainage was practically negative except for an intensely inky black "B" fraction, tar-like in consistency, suggesting an atonic static gall-bladder. This deficiency in function was probably due to the total absence of gastric acids and enzymes, which deprived her of the normal duodenal physiologic stimulus to gall-bladder emptying.

The x-ray report of Dr. Manges stated that there was a perforating ulcer near the cardiac end of the stomach on the lesser curvature, pylorospasm, mobile cecum, incompetent ileocecal valve, and intestinal hypermotility.

Because there were no clinical, historic, or physical suggestions for ulcer it was considered that the x-ray diagnosis of penetrating gastric ulcer might instead be a diverticulum. This might have been produced as a result of the severe paroxysmal coughing and retching accompanying an adult whooping-cough, which, with its diaphragmatic contraction, had acted upon one of the weakest muscular points in the gastric wall, namely, the cardiac lesser curvature. The evidence of this being a diverticulum was furnished by recovering forty-eight-hour retention foods, spinach, etc., in small quantities from the lavaged stomach after the use of astringents.

This patient was treated by lavage and biliary drainage every other day for several weeks, with relative symptomatic improvement. However, two months later she had a severe attack of general abdominal pain, accompanied by diffuse tenderness, with a sense of band-like constriction at the level of the navel. On inspection there could be noted unusual visible peristalsis of

the gut. Following a paroxysm of pain there was observable a palpable and visible knotting and bulging in the left abdomen about 2 inches above and to the left of the navel, drawing up or displacing the gut below this point so that the left iliac artery

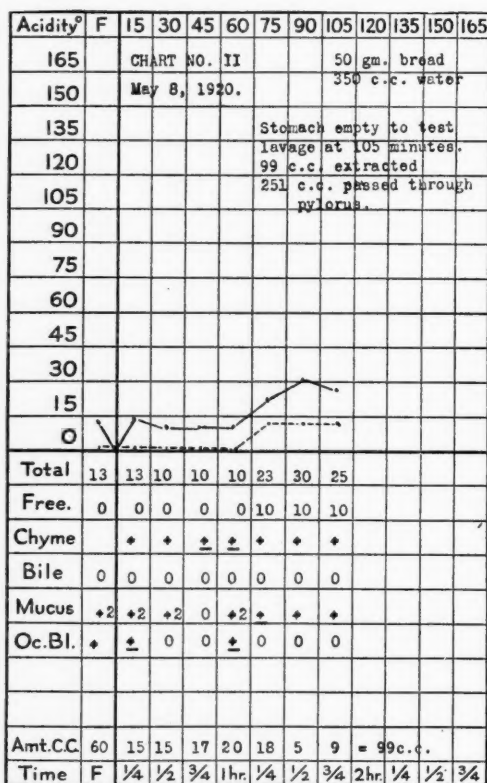


Fig. 138.

was entirely uncovered and easily palpable. Fifteen minutes later this condition had disappeared and the "knot" and left iliac artery were no longer palpable. During the attack the leukocyte count was normal, temperature slightly elevated, and

there was moderate nausea and vomiting with eleven-hour retention.

Volvulus, intussusception, or visceral crisis were considered. The latter was ruled out by negative spinal fluid Wassermanns and cell counts. In view of the *x*-ray and clinical findings, temporary intestinal volvulus from mobile cecum, as a reflex to a chronic appendicitis, was diagnosed.

At operation Dr. Despard found a definitely pathologic retrocecal appendix, its tip pointing toward the gall-bladder, and bound down by adhesions. The gall-bladder and ducts were normal in appearance. There was a structure like a Jackson veil attached to an unusually mobile cecum. The appendix was removed and adhesions separated by careful dissection.

This patient made an excellent postoperative recovery, and inasmuch as she has had no further attacks during the past five years, it is highly probable that the diagnosis was accurate and the surgical procedure adequate.

During the course of her follow-up study, eight months after operation (May, 1920), it was found that her free hydrochloric acid began to appear at seventy-five minutes in appreciable amounts instead of at one hundred and five minutes (Chart II, Fig. 138). Gastric substitution products had been used, and lavage and biliary tract drainage had been carried out at intervals of two to four weeks, the latter to protect a static and atonic gall-bladder. Her bilious attacks disappeared, with steadily improving function of the gall-bladder. Her final recheck, on March 11, 1924, showed a gastric acidity restored to normal limits, with a normal curve (Chart III, Fig. 139).

At the same time, with this it is extremely interesting to note that the "B" fractions now recoverable, instead of being a tarry black and viscid bile, are of perfectly normal color and consistency. This indicates, I believe, that with restoration in gastric function the gall-bladder is no longer deprived of its normal physiologic contraction reflex, which occurs when a meal acted upon by an acid gastric juice is converted into peptones and albuminoses, as shown by the physiologic studies of Rost and confirmed by others. It is likely that the patho-

logic appendix, with unusual adhesions and a mobile cecum, may reflexly have produced the spurious achylia, which, in turn, encouraged gall-bladder stasis.

The special points in this case to which I would invite your attention are:

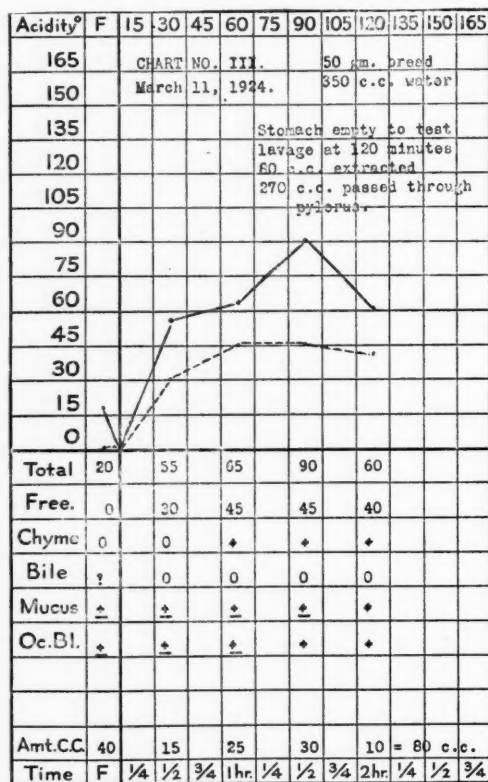


Fig. 139.

First, that a diverticulum in the stomach may be produced by the severe retching of adult pertussis.

Second, that the physiology of the gastro-intestinal tract is intimately interrelated, so that disease or dysfunction in one

organ may reflexly produce malfunction in another quite distant one.

Third, that the only safe way of differentiating the achylia is by fractional analysis; that the nature of the achylia, whether benign or malignant, is suggested by special differential tests; that the prognosis is determined by the demonstration of proenzymes.

Fourth, and finally, this case represents a group for whom prophylactic measures should be adopted for the prevention of later gall-tract pathology.

Notwithstanding considerable adverse criticism, I personally know of no method other than that of biliary tract drainage which can diagnose gall-tract disease or dysfunction in the early stage of disturbed physiology, nor any method of direct treatment which offers as much practical accomplishment in securing not only symptomatic relief, but restoration to normal findings.

In a recent series of 376 consecutive cases, I<sup>1</sup> have reported the remarkable therapeutic value that non-surgical drainage of the gall-tract possesses in properly selected groups. The next four cases illustrate the use of this procedure, associated with vaccine therapy and total management, in inflammatory and infected states of the upper right quadrant. The response secured in these cases is not unusual.

**Case II.**—Three years ago a lady of fifty-two was studied. She was complaining of dull aching pain at the exit of the eighth to tenth right spinal nerves, referred around the right costal margin to the epigastrium, which had begun about three years earlier. These attacks had recurred with increasing frequency and severity, lasting six to twelve hours. They were all nocturnal attacks, wakening her with a sense of epigastric fulness and aching distress at the angle of the right scapula referred to right epigastrium, and were accompanied by explosive belching, heartburn, and voluntary vomiting with terminal bile, which usually ended the attack.

She had had no illness except typhoid fever of eight weeks'

<sup>1</sup>Therapeutic Gazette, November and December, 1924.

duration in 1907, featured by a suggestive cholecystitis relapse, and recurrent tonsillitis, although none for the past thirty years.

On biliary tract drainage study, she was found to have streptococcic cholecystitis, with suggestion of potential cholelithiasis, duodenobiliary adhesions, and exfoliative duodenitis. The suspected source of infection lay in infected tonsils. She was a vagotonic and spasmophilic, showing hyperspasticity of the cardia, pylorus, and sigmoid. There was an associated enterocolitis and intestinal toxemia. Pancreatic studies showed deficient function. Blood showed a leukopenia with focal infection lymphocytosis of 41 per cent. x-Ray a year earlier had been negative for ulcer, new growth, or visible gall-bladder or stones.

Her treatment was as follows: Her tonsils were removed and a hemolytic streptococcus cultured out, and a vaccine prepared from a mixture of this and the streptococcus from the gall-tract, and administered over the next two months. She was given 19 biliary tract drainages between April 21 and July 8, 1921. Much difficulty was experienced in the early drainages in entering the duodenum on account of either pyloric inflammatory edema or adhesions, probably the former.

On admission her record showed a loss of 28 pounds in weight within a year, and during the first sixteen days of treatment she lost an additional 5 pounds. This excited comment, and in view of the difficulties of intubating the duodenum, an x-ray recheck was done by Dr. Manges, who reported a pyloric ulcer with possibility of early carcinoma and a pathologic gall-bladder without stone shadows.

In view of this report, a surgical consultation was held with Dr. John Gibbon and early operation urged because of the possibility of malignancy. This advice was unexpectedly declined by both the patient and her husband. She was then placed on an ulcer management, although there were no clinical evidences of ulcer activity, and the x-ray opinion was considered to be equally legitimately interpreted as deformity from adhesions alone.

At the conclusion of her drainage and vaccine period recheck cultures from the gall-tract failed to recover the strepto-



coccus. She was entirely symptom free within two weeks after instituting treatment.

This patient was followed up carefully for three years by letter. Her replies in January, 1922, 1923, and 1924 have been consistently satisfactory, and state that she has been completely relieved of her distress and that she believes herself to be perfectly well. Within a year she had gained 43 pounds in weight, or 10 pounds more than she had lost.

**Case III.**—Two and a half years ago a lady of thirty-eight was complaining of a dull but constant aching pain under the right costal margin or in the right epigastrium, referred around either rib margin to angle of scapula, more often the right.

Aside from typhoid fever as a child and jaundice at the age of ten, and recurrent attacks of tonsillitis, she had been a strong, robust woman, complaining of nothing until six years earlier, when she began to have attacks of nausea lasting one or two weeks, sometimes followed by vomiting, intermittent moderate constipation, and moderate belching.

For four months the pain described above had been constant during the day, with a sense of distention and weight in the region of the gall-bladder.

Physical examination was negative except for slight tenderness over McBurney's point and the duodenal points, and marked tympany over hepatic flexure of colon obscuring liver dullness. *x-Ray* suggested "adhesions to duodenum probably from gall-bladder; cecum adherent deep in pelvis; probable chronic appendicitis."

Gastric study was negative except for subnormal acidity with sustained terminal curve, suggesting an extragastric lesion. Gall-tract drainage revealed exfoliative duodenitis, dysfunction of Oddi's sphincter, and masked infection in gall-tract, cultures recovering heavy and pure growth of *Staphylococcus aureus*, from "A," "B," and "C" fractions.

While this patient's drainage test showed perfect ability to drain the infected gall-bladder, liver, and ducts, she was selected as a case for surgery in view of the associated chronic appen-

dicitis suggested by x-ray. She was an unusually good surgical risk.

At operation two weeks later the cecum was easily pulled up through an upper right rectus incision and not bound down or fixed in the pelvis, as suggested by x-ray. The appendix was freely movable and without adhesions, but showed evidence of chronic inflammation, which was confirmed by postoperative tissue study. The first view of the fundus of the gall-bladder showed it to be apparently normal, but better surgical exposure found it definitely acutely antileflexed by a veil-like band of adhesions which extended from the neck of the gall-bladder running downward and adherent posteriorly behind the common duct. There were no adhesions between duodenum or gall-bladder, although dense adhesions between the transverse colon and duodenum accounted for the moderately delayed gastric motility as shown by x-ray, and for the dilated hepatic flexure noted by physical examination. There was no evidence of gastric or duodenal ulcer. I had hoped the surgeon might spare this gall-bladder, but in dissecting the adhesions, so much trauma and laceration was occasioned as to make it unwise to leave in the gall-bladder on account of the likelihood of re-formation of more pronounced obstructive adhesions. It was therefore removed by low cystic duct ligation. The adhesions elsewhere were also released. Cultures from the gall-bladder recovered *Staphylococcus aureus*.

This patient made an excellent postoperative recovery until six weeks later, when there occurred a severe attack of upper right quadrant pain, accompanied by nausea and painful aching at the tip of the right shoulder-blade. Then followed several attacks of definite pain of moderate severity, with persistent nausea.

Twelve weeks after operation this patient returned to the city and a recheck drainage showed absence of "B" fraction, but definite duct catarrh, and again a heavy and pure culture of *Staphylococcus aureus* was recovered from "AC" fractions, demonstrating residual infection in ducts or liver. It is important that surgeons realize this and "follow-up" with non-surgical drainage to prevent cholangitis.

In addition, it was quite evident that, from a physiologic standpoint, this patient had not become compensated to the loss of her gall-bladder, for frank biliary regurgitation was found in this patient's fasting stomach on many successive mornings. This indicates dysfunction of Oddi's sphincter, and where reverse peristalsis, secondary to duodenitis, exists, biliary reflux into the stomach takes place. In my opinion this constitutes an important diagnostic sign of gall-tract-duodenal or appendical disease. In badly compensated cholecystectomies, and especially where residual duct infection remains, there is continuous emptying of infected bile into the duodenum, often producing diarrhea and a duodenal irritation, causing reverse peristalsis and frequent biliary regurgitation.

It is suggested that the persistent nausea is produced in this way, since the postoperative technical topical management, consisting of daily aspirations of the regurgitant bile in the stomach, followed by gastric lavage, with weekly or, in certain more extreme cases, daily or every other day drainage of the ducts and liver, followed by duodenal disinfection and transduodenal lavage, has served in a large series of cases to bring about a final and complete recovery, although it may take from four to six months to accomplish this result. But this is better than having to undergo multiple operations.

This plan of management combined, as usual, with the use of an autogenous vaccine, was carried out with this patient, whose attacks gradually disappeared. It is to be noted that injections with this vaccine were followed by definitely focalizing reactions felt in the upper right quadrant, producing an exacerbation in pain, and sometimes nausea and vomiting. This is a favorable sign, as I have reported elsewhere, inasmuch as it seems to indicate the specificity of the bacteria in the vaccine.

In January, 1923 a recheck culture showed a disappearance of the *Staphylococcus aureus*, which has never returned. At her last bi-annual visit in September, 1924 her drainage findings were perfectly normal, and she states that she is perfectly well, although she still persists in her self-conducted home drainage

every four to eight weeks, insisting that this procedure adds to her comfort.

*Discussion.*—The query is advanced as to whether such a plan of management is justifiable in view of the fact that non-surgical drainage may have to be kept up for a considerable period. My experience has shown that it is an excellent method of preventing postoperative relapses, especially where it is evident that the liver or ducts still harbor a pyogenic infection, since it serves in the most practical sense to protect the liver and to prevent a postoperative cholangitis, which, in another series of cases, has been found to occur far too frequently. The larger majority of my cases have shown that the topical treatment can be discontinued comparatively early. Practically all patients, when trained, have found that this therapeutic drainage procedure can be carried out by themselves, and if it serves to increase their physical comfort, is it not as justifiable for them to do this as to take an occasional vaginal douche or topical treatment of the nose or throat in order to prevent the necessity of again undergoing major surgery?

That this postoperative discomfort of upper right quadrant pain attacks, associated with nausea and vomiting, is not confined alone to my series of cholecystectomized cases, is shown by the fact that I have found a very similar state of affairs to exist in a large percentage of my cholecystostomized cases, when they "go wrong," as is evidenced by the following case report.

**Case IV.**—One and a half years ago a young woman of twenty-eight was complaining of right costal margin ache and sense of distention and dull pain at the tip of the right shoulder-blade. A cholecystostomy had been done in December, 1921, at which time gall-stones had been removed, adhesions released and the gall-bladder drained for twelve days. The appendix was also removed. Four years previous to operation she had had periodic attacks of acute cramp-like pains in the upper right quadrant, referred to the right shoulder-blade, accompanied by "generally upset stomach." There was also much belching and continued constipation. These attacks lasted for four days to

a week or more. Five months after operation she had a return of the same symptoms, putting her to bed for a week. She rested all summer, and although there were no further attacks, she felt so miserable that she was not able to work the following winter.

In February, 1923 she had a severe attack of pain followed by jaundice lasting two weeks. Again in April another attack led her to present herself for study. She had lost about 35 pounds in weight to a low point of 115. Being a congenital viscerototic, this loss of weight aggravated all of her symptoms. More recently, since operation, she had developed very severe supra-orbital, prostrating, sick headaches, associated with nausea, which lasted for several hours, although the following day she felt better and more clear headed than before the headache was inaugurated.

On physical examination she showed marked relaxation of her vasomotor system, low blood-pressure, cold, sweating hands, and pronounced tache and dermatographia. Abdominally, her aorta and right iliac artery were uncovered and tender. There was also definite tenderness at the top of her midright rectus scar. Tuning-fork test was positive from stomach through liver and suggested adhesions between duodenum and under surface of liver. She had definite tender points over the right spinal nerves emerging between the fifth and eighth thoracic vertebræ.

Her tube studies showed a subacid gastric curve with pronounced biliary regurgitation in the fasting and digesting states. Pancreatic tests were normal. Biliary drainage showed a catarrhal exfoliative duodenitis with pronounced bile-duct catarrh, but no cultural evidence of pyogenic infection, although a light *Bacillus coli* recovery was obtained. There was persistent dysfunction in a relaxed Oddi's sphincter, with continuous bile discharge into the duodenum. The "B" fractions showed a heavy black brown bile containing moderate catarrhal and inflammatory elements, together with an increase in pigment crystals and bile salts.

Her intestinal motility was delayed to sixty-eight hours, notwithstanding mild laxatives. x-Ray examination by Dr.

Manges of the gastro-intestinal tract suggested no organic lesion, although there was slight flattening of the duodenal cap, interpreted as due to adhesions. There was also moderate gastric retention, due to pylorospasm, and intestinal delayed motility, especially in the ileum.

In view of the fact that this young woman was desirous of perfecting her laboratory training as technician, she was engaged as part time assistant in order to give her an opportunity for closer management.

Her treatment was outlined as follows: A modified home visceroptotic management with Curtis pad, elevation of foot of bed, and definite rest periods; bland diet on the five-meal plan and the use of tonics; daily lavage and biweekly gall-tract drainage, with transduodenal lavaging enemas. She was given twenty drainages between April 26 and December 18, 1923. By July she was symptom free and went through the summer with steadily increasing health, and by November had gained from 115 to 136½ pounds. Her headaches were entirely controlled after treatment was well established.

She was then considered well enough to go on an interval drainage of three months, and changed her scene of employment. This interval apparently is too long to maintain her symptom free, for she has had a slight return of nausea and upper right quadrant distress, although her drainage findings are objectively greatly improved.

It should be remembered, however, that this postoperative plan of drainage was not inaugurated until sixteen months after her operation, and, in view of the evident persistence of a cholecystodochitis, additional late pathology, in the form of recurrent adhesions, and so on, had had time to take place, and it is quite possible that the future will show that this plan of management will not prove effective in her case and that reoperation may have to be advised. Nevertheless, she has been restored to a much better condition of general health, and at the same time has had her gall-tract better prepared, so that if operation should prove to be desirable, she will be in much better shape to go through it now than a year ago.

I am convinced that when these follow-up plans of non-surgical drainage are proved indicated by postoperative study of a gall-tract case, and are inaugurated shortly after operation, much better results can be obtained. This is shown by the following case, illustrative of this group.

**Case V.**—Three years ago a lady of thirty-nine presented herself with a long history of stomach trouble dating back to childhood, when she used to crave acids and sour things, and drank vinegar by the spoonful "because she liked it." She was subject to train sickness and seasickness, and to recurrent tonsillitis.

On total study it was found that she represented a case of multiple gastro-intestinal lesions masquerading under the duodenal ulcer syndrome. This is a far more common occurrence than has formerly been emphasized, and is one of the important lessons which has been learned after studying large groups of chronic digestional invalids.

To a typical history of one- to three-hour postmeal hunger-pain, and nocturnal distress relieved by food or alkalies, there were superimposed attacks of nausea and vomiting and right subcostal margin pressure distress and shoulder-blade ache, accompanied by jaundice; in addition there was quite definite tenderness over McBurney's point, as well as gall-bladder and duodenal points, during and between these attacks. Tuning-fork test suggested adhesions between duodenum and gall-bladder.

That this represented late pathology is shown by the fact that all three lesions were demonstrable by the x-ray examination of Dr. Manges. Very often associated ileocolitis accompanies such cases.

Gall-tract drainage delivered pathologic biles with static "B" fractions and microscopically showed a pronounced catarrhal and inflammatory cholecystodochitis, with intermittent exacerbations of subacute cholangitis. The cystic duct was not obstructed. Cultural recoveries of *Staphylococcus aureus* and *Bacillus coli* were obtained.

At operation by Dr. John Gibbon the following pathology was demonstrable: Retrocecal appendix kinked by adhesions to mesentery of lower ileum; scar of old and apparently healed ulcer on anterior surface of duodenum immediately below pyloric ring; old dense adhesions between first portion of duodenum and lower third of inferior surface of gall-bladder and liver, and dense adhesions between middle third of inferior surface of gall-bladder to gastrocolic omentum. Gall-bladder bluish gray, tense, not thickened, and emptied under digital pressure. Appendix removed and pyloroplasty performed. Gall-bladder opened, mucosa swollen and inflamed, not strawberry type. Bile thick, greenish black. No stones found. Cultures recovered *Bacillus coli* and *Staphylococcus aureus*. Gall-bladder swabbed out with gauze, drained with large rubber tube. Moderately stormy postoperative recovery during first ten days, thereafter uneventful.

On discharge from the hospital this patient was given the usual surgical follow-up procedures of cholegogue or saline laxatives designed to flush out the bile-ducts and prevent cholangitis relapse. That this is often ineffectual therapy is evident by the fact that six weeks after operation recheck drainage still showed a catarrhal exfoliative cholecystodochitis with persistent recovery of *Staphylococcus aureus*. Eight postoperative drainages, with vaccine therapy, served to clear up all of the remaining abnormal objective findings. A recent letter states that this patient two and a half years later is in perfectly good health.

*Discussion.*—It was decided to try to save this particular gall-bladder inasmuch as its function was not notably impaired. This represents a type of gall-bladder disease upon whom more conservative surgery can be practised provided non-surgical drainage is postoperatively carried out wherever indicated. I can strongly recommend that such a follow-up plan of management be used, for our experiences with such cases have been far more satisfactory and have shown less frequency in postoperative relapses.

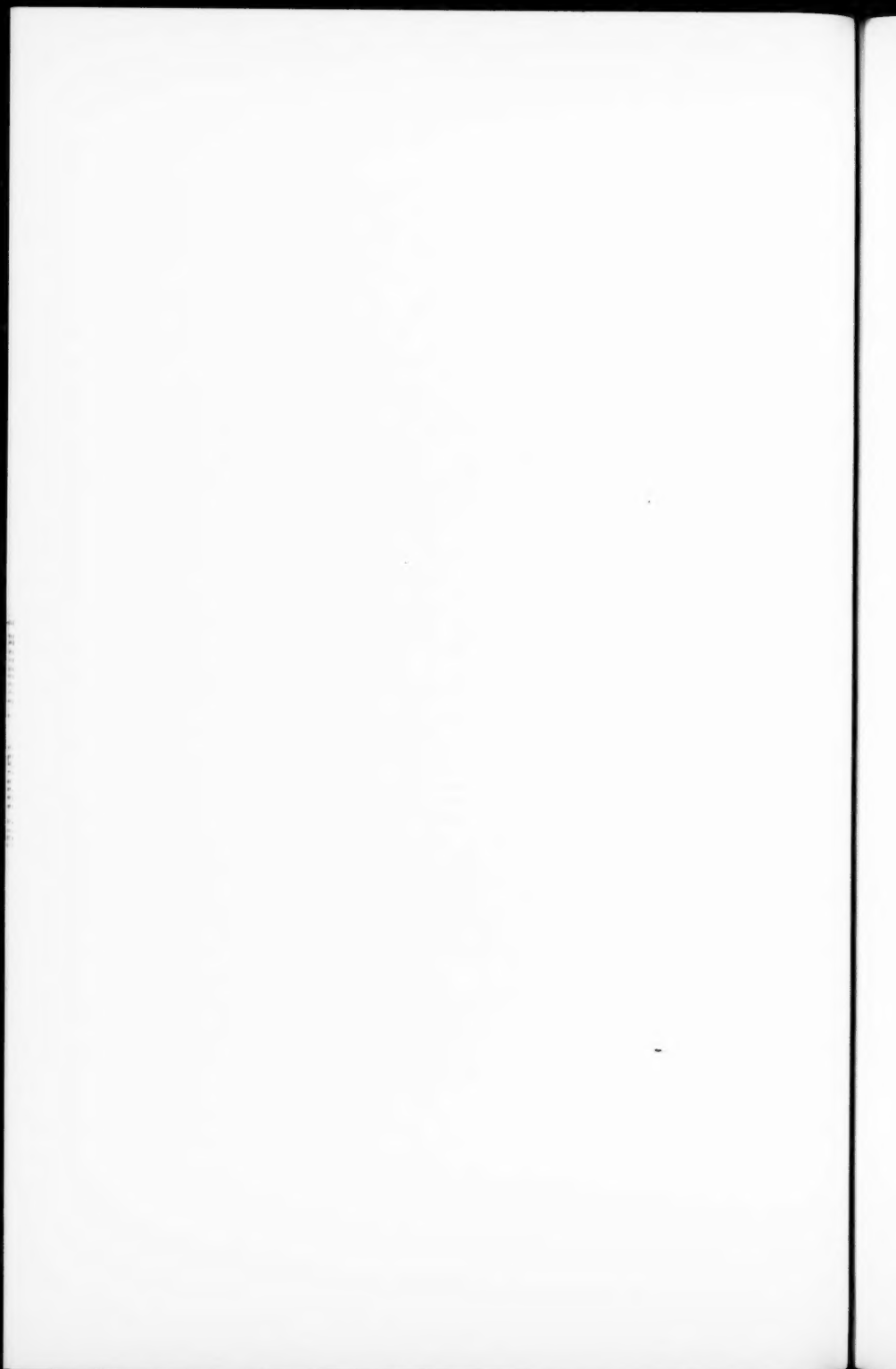
I wish to again call attention to the frequency of multiple lesions, simultaneously coexistent, in the gastro-intestinal tract,



which can be determined by a total diagnostic survey of the patient. I believe that infection is the commonest single cause of such multiple lesions and may produce disease of the stomach or duodenum, of the gall-bladder, the appendix, and often the ileocolon. In most cases these multiple lesions are furnished from the same infective source, usually found within the mouth or upper respiratory passages.

I consider it poor judgment to undertake the treatment of any chronic or subacute duodenal ulcer, cholecystitis or choledochitis, or of any chronic appendicitis, cecitis, or ileocolitis, whether this treatment be by a surgical or medical, or combined plan, until *after* all extragastric foci of infection, especially those in the mouth, have been eradicated. How very frequently we see recurrent or relapsing duodenal or marginal ulcer, when pus and bacteria discharging tonsils, gums, or teeth are left behind, in a patient upon whom a gastro-enterostomy has been done, after several half-hearted attempts to use a definite plan of medical management have likewise failed!

Finally, we should all realize that surgical measures have their limitations and non-surgical measures theirs, but, by combining them intelligently, we can do more to prevent alimentary tract disease, as well as to cure or improve both its early and late stages.



CLINIC OF DR. RICHARD A. KERN

UNIVERSITY HOSPITAL

PROBLEMS OF CLINICAL HEMOGLOBIN ESTIMATION

- (a) THE selection of a clinical method.
- (b) Colorimeter standards.
- (c) Accurate check by determining oxygen capacity.

DR. KERN: You say the blood-count of this patient is suggestive of a primary anemia. What are the figures?

STUDENT: The red cells number 2,500,000, the hemoglobin is 55 per cent., and the color index 1.1.

DR. KERN: The hemoglobin is 55 per cent. of what?

STUDENT: 55 per cent. of normal.

DR. KERN: And what is "normal"?

STUDENT: The average amount of hemoglobin found in the blood of healthy adults.

DR. KERN: And is that a fairly constant figure?

STUDENT: I think not. I know it varies with sex; in men it is 90 to 100 per cent., while in women it is around 80 or 85 per cent.

DR. KERN: Again I ask, percentage of what? Can you give an absolute figure for normal hemoglobin content of the blood, say in terms of grams of hemoglobin per 100 c.c. of blood?

STUDENT: I think it is about 15 grams.

DR. KERN: Perhaps; we will discuss that a little later. With what instrument did you obtain your hemoglobin reading?

STUDENT: With a Sahli hemoglobinometer.

DR. KERN: And how many grams of hemoglobin per 100 c.c. of blood does a 100 per cent. reading with this instrument indicate?

AVERAGE STUDENT (and probably also average doctor): I don't know.

DR. KERN (to the class): Can anyone tell me?

The correct answer is promptly volunteered by that paragon of scientific information, the Super Student of Medical Clinics: 17.3 grams hemoglobin per 100 c.c. of blood, a top normal figure, and found only in robust young adult males.

In that case, is it not incorrect to compute a color index directly from the Sahli hemoglobin reading?

SUPER STUDENT: Yes, Sahli uses a corrected reading in computing the color index. The hemoglobin reading of normal males varies from 80 to 100 per cent. with this instrument, and the average of these extremes, or 90 per cent., is considered as 100 per cent. of average normal. A reading of 55 per cent. on the instrument would therefore correspond to a corrected reading of  $55 \div 90 = 60$  per cent. of normal, and the color index in our patient would be  $\frac{60 \text{ (per cent. of hemoglobin)}}{50 \text{ (per cent. of cells)}} = 1.2$ .

DR. KERN: Yes, a figure that is rather more suggestive of primary anemia.

At this point the intern, who has been showing increasing signs of restlessness, breaks into the argument: Pardon me, Dr. Kern, the last lot of standards for the Sahli instruments were made up to represent 14 grams of hemoglobin per 100 c.c. of blood. The corrected reading would therefore not be 60 per cent. of normal, but  $14/17.3$  of 60, or about 49 per cent., and the color index of our patient is actually a little less than 1.

Thus is confusion worse confounded!

Hemoglobin estimation is the most frequently performed of the clinical examinations of the blood. Unfortunately, and largely because of lack of uniformity in standards, the results have also the least absolute value.

For many years the color of the blood has been the subject of clinical examination and speculation. In the seventeenth century when blood letting was in its hey-day much was written on the color of the blood before and after clotting in various states of health and disease, but the observers of that day, handicapped by the lack of adequate methods of examination, could note only the grossest changes. Little wonder, therefore,

that the clinical conclusions drawn from the inspection of venesection blood amounted to little more than empty hypotheses and conjectures.

But with the great advances that chemistry and physics experienced from the start of the nineteenth century, an accurate knowledge of the blood and its constituents grew apace. From the discovery by Berzelius in 1808 of iron as the basis of the coloring-matter of the blood, there was sound steady progress, step by step, to the work of Hoppe-Seyler, who recognized the specific oxygen-combining power of the iron and gave hemoglobin its name. Chemical and physical researches showed that the composition of hemoglobin is constant in health and disease. Its quantity might be accurately determined therefore by measuring its iron content or its oxygen capacity. Nearly fifty years ago Vierordt applied the discovery of quantitative spectroscopic analysis to the quantitative estimation of hemoglobin, and it still is our most accurate method.

But none of these methods were available for routine bedside work. They all were open to one or more of these objections—costly apparatus, large quantity of blood needed, time-consuming and difficult procedure.

The clinician, therefore, developed another group of methods, based on colorimetry. To Ehrlich has been attributed the simple expedient of comparing a drop of the patient's blood with a drop of normal blood on a bit of cloth. Tallqvist, elaborating on this, prepared a chromolithographic scale, corresponding to the shades given by a drop of blood caught on a filter-paper. There is an arbitrary normal set at 100 per cent., and a series of lighter shades differing by 10 per cent. However, only marked differences can be determined and the method has a limit of error up to 25 per cent.<sup>1</sup>

What are the requirements that a practical clinical instrument for hemoglobin determination should fulfil? It is reasonable to demand that: the method should be simple, requiring little time and a small quantity of blood. It should be reasonably accurate with a limit of error of not more than 5 per cent.

<sup>1</sup> Liebmann, *Zentralblatt f. Inn. Med.*, 1917, 38, 449.

Readings should be possible by artificial light as well as daylight. Standards should conform to some absolute hemoglobin value so that their correctness may be determined from time to time. It is desirable that the instrument be simple and cheap, and parts easy and cheap to replace, especially the standard.

Hemoglobin colorimeters fall into two groups: Those in which the blood is compared with an artificial standard and those in which the standard is prepared from blood. Many instruments of the former type have been devised. Gowers<sup>1</sup> described the first clinical hemoglobinometer. He used a dilution colorimeter, with a picrocarmin solution as a fixed standard, graduated in percentage of an arbitrary normal color. Fleischl dissolved a given amount of blood in a fixed quantity of water and compared the color of the solution with that of a colored glass wedge mounted in connection with a scale graduated in percentage of normal. In the Dare instrument a thin layer of blood between glass plates is compared with a colored glass standard. The Tallqvist scale has been mentioned. Newcomer uses colored glass plates to compare with the unknown blood, converted into brown acid hematin by decinormal hydrochloric acid, while the Autenrieth-Koenigsberger instrument employs a hollow glass wedge containing a suitable colored solution.

What are the objections to these instruments with artificial standards? These vary with the instruments; some have one fault, some another, but all are open to one fundamental criticism. It is an optical principle that color comparison of like solutions is more accurate than comparison with an artificial color approximation. It is easier to reproduce the brown color of acid hematin than the red shades of laked blood, and therefore such instruments as the Newcomer and Autenrieth-Koenigsberger achieve results that are sufficiently accurate. Yet even here error may creep in, because when hemoglobin is treated with hydrochloric acid the resultant acid hematin is not in solution, but in suspension in a state of extremely fine division. The fluid is therefore slightly cloudy, while artificial glass or solution standards are clear. Glass wedges colored to match laked blood

<sup>1</sup> Trans. Clin. Soc., London, Lancet, 1878, 2, 882.

are often very inaccurate. Senty<sup>1</sup> claims that results with the standard Dare instrument over 70 per cent. of hemoglobin are very misleading and no more accurate than the Tallqvist. With the Fleischl hemoglobinometer there is the additional disadvantage that the blood-measuring pipets are often inaccurate, and the writer has seen readings with two instruments on the same blood differ by 30 per cent. Artificial standards are usually made for use with artificial light only or with daylight only, and a change to the wrong illumination increases the chance for error. Only a few artificial standards are made to correspond to a given absolute value in grams of hemoglobin per 100 c.c. of blood. This is true of the Newcomer glass plate (100 per cent. = 16.9 grams hemoglobin per 100 c.c.) and the Autenrieth-Koenigsberger. Artificial standards made of glass are more costly than solution standards, while the latter have the added advantage that they can usually be easily prepared in any well-equipped laboratory.

Let us consider now methods in which blood is used in making the standard. Aqueous solutions of hemoglobin rapidly deteriorate and therefore cannot be used, but acid hematin suspensions if prepared under aseptic precautions and if kept in the dark will hold their color unchanged for two years.<sup>2</sup> Sahli makes use of this in his modification of the Gowers dilution colorimeter. He uses as his standard an acid hematin suspension corresponding to the top normal hemoglobin values found in robust young adult males, and equivalent to 17.3 grams of hemoglobin per 100 c.c. of blood. The instrument possesses certain excellent advantages. It is simple, compact, and accurate to 5 per cent. It can be used by daylight or artificial light. The standard is fairly permanent, and if broken or faded, can be replaced easily. Almost every hospital laboratory is sufficiently well equipped to make up new and accurate standards.

Several disadvantages of the Sahli instrument can be pointed out. It is too small for readings of great accuracy, it is true, but there is no particular advantage in readings closer than 5

<sup>1</sup> Jour. of Lab. and Clin. Med., June, 1923, 8, 591.

<sup>2</sup> Bürker, Münch. Med. Wehnschr., 1912, 59, 14, 89.

per cent. in ordinary clinical work. When greater accuracy is needed much more refined methods and costly apparatus (larger colorimeters, oxygen capacity determinations) must be used and hemoglobin estimation is no longer a bedside but a laboratory procedure. With a dilution colorimeter the procedure is not reversible and only a single reading can be made with one blood sample. This is a very real objection and various attempts have been made to obviate this difficulty. Haden<sup>1</sup> dilutes the blood always to the same degree and then compares with the standard acid hematin suspension in a glass wedge. For this purpose he uses the ordinary Hellige colorimeter. The procedure is accurate and sufficiently simple for bed-side work. The instrument is, however, more elaborate and much more costly than is desirable for routine clinical bed-side work. The same objection applies in still greater degree to several other methods (*e. g.*, Cohen and Smith<sup>2</sup>) which use acid hematin standards with various types of colorimeters. The Sahli type of hemoglobinometer is, after all, probably the best adapted for the purpose.

At this point it seems worth while to warn against certain errors in technic that may give rise to incorrect readings. In the first place the blood must flow freely from the finger, without pressure or only very slight pressure. Much squeezing gives an excess of serum over cells and the hemoglobin reading will be too low. When blood is treated with decinormal hydrochloric acid the change from hemoglobin to acid hematin is not instantaneous, but proceeds gradually, with a gradual darkening of the brown color. In the Sahli method acid is put in the graduated tube up to the mark 10, and blood is added by means of the pipet provided. Then water is added drop by drop and mixed until the color matches that of the standard. It is necessary to wait a full minute for the brown color to develop before adding the water. Some observers, using very accurate colorimeters, have claimed that the color continues to darken for fifteen to twenty minutes, and that for absolutely accurate

<sup>1</sup> Clinical Laboratory Methods, St. Louis, 1923, p. 89.

<sup>2</sup> Jour. Biol. Chem., 1919, 29, 489.



results one should wait fully fifteen minutes before making a reading. Sahli himself has answered this criticism by pointing out that in some of these experiments the entire dilution was carried out with hydrochloric acid instead of water, which will cause a slightly darker color than when water is used. Even so, the maximum error claimed against too early reading is only 4 per cent., or within the limit of error of the method. To repeat: Let the blood-acid mixture stand a full minute before proceeding to dilute, and use water, not acid, for the further dilution. The standard should always be shaken before using to insure the proper color. The acid hematin is in very fine suspension (not solution) and tends to settle out, leaving a lighter colored supernatant fluid. If these points are observed a reading accurate to 5 per cent. is obtained. Readings closer than 5 per cent. are not possible and they should therefore be recorded only in multiples of 5.

What of the calibration of the standard? In the last analysis the only correct statement of hemoglobin content of the blood is in terms of absolute percentage, that is, in grams per 100 c.c. Such a terminology is used in every other chemical analysis of the blood (sugar, urea N, uric acid, etc.), and it would be only logical to so graduate hemoglobinometers. But the common use of terms in percentage of a supposed normal 100 per cent. of hemoglobin has been employed for a definite purpose, namely, the expression of the relation between the erythrocyte count and the hemoglobin content, *i. e.*, the color index.

What is the normal 100 per cent. of hemoglobin? This is a vexatious question to which many answers have been given. Such a "normal" amount would presuppose that in health there is a constant hemoglobin charge per individual erythrocyte. Many hematologists have concluded that this is not the case. Certainly there are wide variations in the amount of hemoglobin per 100 c.c. of blood as found at different ages, or in males and females at the same age, or even in the same individual at different times of the day. As early as 1878 these facts were clearly shown by Leichenstern,<sup>1</sup> and they have been abundantly con-

<sup>1</sup> Hemoglobulingehalt des Blutes, Leipzig, 1878.

firmed. Williamson<sup>1</sup> made spectrophotometric hemoglobin readings in over 900 healthy individuals, about half of them in each sex and in successive age groups from one day to over seventy-six years. The highest figures are obtained at birth (about 23 grams per 100 c.c.); then they rapidly fall to a minimum (12.4 grams) in the second year. There is a gradual rise up to the sixteenth year, with practically no difference in the sexes. From sixteen to fifty-five the average values are fairly constant, 16.92 grams for males and 15.3 grams for females. After fifty-five there is a slight decline, figures for women continuing lower than those for men. At a glance one might readily say there is no normal value.

Yet the question has recently been reopened. Haden<sup>2</sup> made a series of erythrocyte counts and hemoglobin estimations by the van Slyke oxygen capacity method in 20 males, ages eighteen to thirty; 20 males, ages thirty to fifty; and in 12 females, ages twenty to forty. He then calculated the amount of hemoglobin on the basis of a 5,000,000 erythrocyte count, obtaining an average of 15.57 grams per 100 c.c. in the first group, 15.65 grams in the second group, 15.65 in the third group, with an average for all of 15.6 grams per 100 c.c. for a 5,000,000 red cell count. The variations from the average in individual cases were remarkably slight. The color index showed maximal and minimal values of 1.05 and 0.95 respectively, quite within the limits of error of the determination, while the average was exactly 1.00. Williamson made no blood-counts on his subjects, but if his figures are recalculated on an assumed cell count of 5,400,000 for males and 4,700,000 for females, the average hemoglobin figure for 5,000,000 cells would be about 15.8 grams, not far from Haden's results.

It is also interesting to note that Sahli advised as an arbitrary normal for color-index calculation the 90 per cent. level of his hemoglobinometer scale. *i. e.*, 90 per cent. of 17.3 grams, or 15.57 grams.

<sup>1</sup> Archives of Internal Medicine, 1916, 18, 505.

<sup>2</sup> Jour. Amer. Med. Assoc., 1922, 79, 1496; Archives of Internal Medicine, 1923, 31, 766.

It is a significant fact that a normal sized erythrocyte cannot contain a hemoglobin quantity appreciably exceeding the normal charge. It is a common mistake, for instance, to suppose that the high-color index of primary pernicious anemia is due to an excessive amount of hemoglobin in a normal cell volume. This is not true. The total red cell volume percentage in primary pernicious anemia is always above the normal for a given cell count, and this volume increase is greater proportionately than the hemoglobin increase, so that even in primary pernicious anemia, the individual erythrocyte as a rule actually contains less hemoglobin than the normal red cell *per unit cell volume*. This was shown by Capps<sup>1</sup> in his observations upon the volume of erythrocytes in this disease, and has been confirmed by Haden.<sup>2</sup> Gram and Norgaard<sup>3</sup> also found such a constant relation in normal blood between the cell volume and the hemoglobin content that they feel justified in computing the one from the other.

Myers<sup>4</sup> says: "Excepting such blood diseases as pernicious anemia and chlorosis, where the hemoglobin content of the cells may be increased or decreased respectively, thus giving rise to a high or low so-called 'color index,' the hemoglobin parallels fairly closely the number of red cells, and consequently furnishes little added information." Morris<sup>5</sup> in his text-book recommends Haden's figure of 15.6 grams of hemoglobin per 100 c.c. as the 100 per cent. normal for 5,000,000 erythrocytes.

Practical purposes and some good clinical evidence therefore both argue for the adoption of 15.6 grams as the standard normal for a 5,000,000 red cell count. Its use in the Sahli instrument would obviate the need for recalculation to obtain a color index, since it could be calculated directly. The universal adoption of such a standard would give to all clinical hemoglobin estimations a value for comparison that they do not now possess.

<sup>1</sup> Jour. Med. Research, December, 1903, 10, 307.

<sup>2</sup> Loc. cit.

<sup>3</sup> Arch. Int. Med., 1923, 3, 164.

<sup>4</sup> Practical Chemical Analyses of Blood, St. Louis, 1924, p. 164.

<sup>5</sup> The Clinical Laboratory Diagnosis, New York and London, 1923, p. 264.

Since hemoglobin readings in the average case give little additional information if the red cells have been counted, it might appear that hemoglobin estimation need not be a routine procedure. Quite the contrary is true. If we know that our hemoglobin reading is accurate to 5 per cent., then it has a greater value than ever as a check in the normal case on red cell figures, and as a diagnostic help when the color index varies from unity. The very ease with which the test can be made is enough to make it a part of every blood examination. Finally, it gives a renewed assurance to the practitioner to realize that so simple a test, requiring only a few minutes and little material, applicable in all places and on all occasions, has an accuracy to 5 per cent.—250,000 in terms of red cells, or nearly as small a variation as we consider insignificant even in careful erythrocyte counting. Hemoglobinometry should have a wider application than ever.

What use shall the clinician make of the more accurate and complicated methods of the laboratory? For years the efforts of those engaged in laboratory research has been to simplify analytic procedures without at the same time sacrificing accuracy. Van Slyke<sup>1</sup> has in a large measure succeeded in doing this for the Haldane method of hemoglobin estimation by determining its oxygen capacity. The method is not of great technical difficulty and can be performed in twenty-five to thirty minutes. The apparatus used is the same gas buret that is used in the estimation of carbon dioxid capacity of blood, an instrument that since the recent universal advances in the study of acidosis, especially diabetic acidosis, is found in practically every hospital laboratory.

Here then is a method of great accuracy, not unduly difficult or time consuming, to which the clinician may turn on occasions. Its chief value lies in the fact that by means of it he can at all times get a check on the accuracy of his routine colorimeter standards. With its help new acid hematin standards can be readily prepared whenever needed.

Finally, to make assurance doubly sure, the clinician may occasionally wish an absolutely accurate hemoglobin reading, not

<sup>1</sup> Jour. Biol. Chem., 1921, 49, 1.

open to the possible error of a personal equation (an error that may creep in in any colorimetric method). It is, of course, neither feasible nor necessary to take 5 c.c. of a patient's blood and measure the oxygen capacity every few days in every case of severe secondary anemia, primary pernicious anemia, chlorosis, or polycythemia, but it can be done, and such a case can be made the occasion for checking up on colorimeter standards by a single oxygen determination.

*To summarize:*

1. The Sahli type of hemoglobinometer is best adapted for routine bedside hemoglobin estimations, because

(a) It is simple, easy to use, inexpensive, accurate to 5 per cent., and serviceable both in daylight and artificial light, while

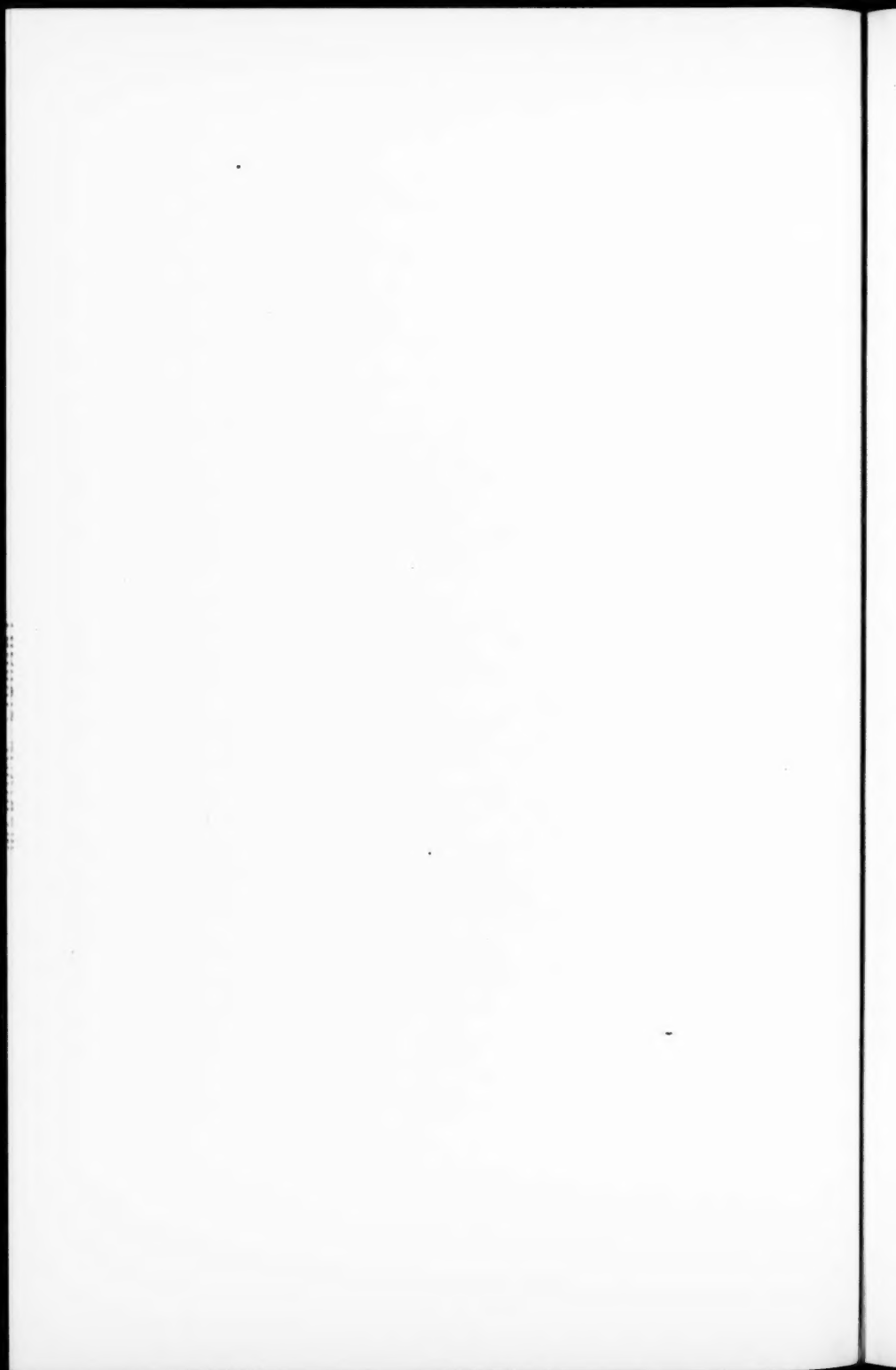
(b) Its standard is reasonably durable, can readily be checked as to its accuracy, and can be made satisfactorily in the average hospital laboratory.

2. Hemoglobin estimation by this method should be a part of all routine clinical blood examination. The practitioner should consider the method as one of the most valuable of clinical procedures at his command.

3. Hemoglobinometers should be graduated in absolute values of grams of hemoglobin per 100 c.c. of blood as well as in per cent. of an assumed normal.

4. 15.6 grams of hemoglobin per 100 c.c. of blood with a count of 5,000,000 erythrocytes (20.9 volumes per cent. oxygen capacity) is endorsed as a figure to represent "100 per cent. normal" for practical hemoglobinometry.

5. The Van Slyke oxygen capacity method for the estimation should be used in every clinic because it combines great accuracy with ready availability and the simplest technic of the really accurate hemoglobin methods. It should find its chief application in the calibration and preparation of proper standards for clinical colorimeters. An occasional oxygen determination in cases of severe anemia or polycythemia will be valuable both in diagnosis and as a check on routine hemoglobin estimations.



## CLINIC OF DR. EMORY G. ALEXANDER

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### CONGENITAL INFANTILE HYPERTROPHIC STENOSIS OF THE PYLORUS

OUR knowledge of this interesting clinical entity is a matter of comparatively recent years. While it is true that cases of hypertrophic stenosis of the pylorus in adults were frequently described in the early literature, their pathology differs from that of the congenital type occurring in infants. That this congenital condition and its surgical cure had scarcely been recognized until the later decades of the nineteenth century is evidenced by the fact that Thomson, in 1897, was able to collect only 15 cases from the literature. The earliest case on record is probably that described by Beardsley in 1788. We again hear of it in a paper published by Williamson, of Leith, bearing the title "A Case of Scirrhus of the Stomach, Probably Congenital," and again in 1842 and 1843 in publications by Dawosky, who seems to have come closer to the modern view of the condition, inasmuch as his article is entitled "Observation on the Hypertrophy of the Submucous Cellular Tissue of the Pylorus, in an Infant Aged Six Weeks." Landerer in 1879 published a case report, but to Hirschsprung is generally conceded the credit of the first actual description of the pathology of the disorder.

**Etiology.**—While early speculation as to the fundamental cause of the abnormal condition took on various aspects, it cannot be said that any one of the earlier theories has stood the test of time, nor that even today there exists unanimity as

to its actual cause. Investigators of the later decades of the nineteenth century, notably Lesshaft, were inclined to find some connection between it and atresia of the duodenum, since the upper part of the duodenum, as pointed out by Hirschsprung, is a favorite site for congenital stricture and complete obliteration. Hirschsprung noted the simultaneous occurrence of dilatation of the esophagus and of the stomach with congenital hypertrophic stenosis of the pylorus, which he took as an indication that the influence of pyloric stenosis was already active *in utero*. Thomson offers the following theory. He believes that the increased musculature and the resulting stenosis is due to overactivity of the muscle begun in intra-uterine life, and that this hypertrophy is due to the swallowing of large quantities of the amniotic fluid. Although this may be slight, yet its constant recurrence, together with the activity of fetal tissues, may in time lead to marked hypertrophy. The essential lesion, according to Thomson, is not a muscular affection, but a nervous one, that is to say, a "functional disturbance of the nerves of the stomach and pylorus leading to ill-co-ordinated and therefore antagonistic action of their muscular arrangements," and that this antagonistic spasm of the pylorus must be "connected with the downward passage of large quantities of liquor amnii, which the fetus is supposed to swallow during the later months of intra-uterine life." The more modern view ignores the possibility of primary pathologic over-development of the muscle, but seems to incline toward regarding the hypertrophy as the result of faulty embryonic development which leads to an actual stenosis of the pyloric orifice, a condition which occasionally is demonstrable at operation, the hypertrophy of the muscle in turn being due to the increased effort required to force the food from the stomach into the duodenum. In other words, as pointed by H. C. Deaver, a compensatory hypertrophy. Deaver differentiates the disorder from pylorospasm in that in the latter the hypertrophy is not compensatory, there being no primary stenosis, and that it is due rather to disturbed secretion. These cases respond to regulation of feeding and to medication, which true hypertrophy does not, as a rule. Even though, as



Deaver remarks, a primary stenosis cannot be demonstrated in every case, it is more reasonable to assume such a condition than that of a primary muscular hypertrophy or nervous derangement as the factor in the etiology of the disease."

Thomson, in a recent discussion of the subject, believes the blocking of the pylorus to be due, first, to the abnormal muscular contraction, and obvious factor, and second, to the mechanical effect of the increased bulk of the muscular tissue, a factor not so obvious, but which he thinks deserves some consideration. The growth of the muscular coat is a rapid one, while that of the peritoneal tube is slow, compared with the general growth of the body, and is capable only of moderate distention. Thus the muscle, as it thickens presses inward and causes elongation and narrowing of the tube of mucous membrane until the gradual increase in the thickness of the muscle is such that even in a relaxed state it embarrasses the functional opening of the pylorus and produces the characteristic symptoms. The development of the hypertrophy being slower in some children than in others accounts for the variation in age at which the obstructive symptoms appear.<sup>1</sup>

The disease apparently shows a predilection for the male sex, and according to some authors affects the little boy more seriously than the little girl. In our series of 107 cases, 90 per cent. were males. The child very often is the first-born infant, although a familial occurrence is not unknown. The symptoms may develop at any time from the seventh or eighth day to the sixth or eighth week of life or beyond that.

The average age of the children coming to operation is about nine weeks, the youngest in our experience being eight days old.

The fact that most of the babies are breast-fed infants excludes faulty diet as a possible cause of the condition.

Diagnosis in most cases is not difficult, the most characteristic symptom being the persistent projectile vomiting.

**Symptoms.**—The chief objective symptoms are vomiting

<sup>1</sup> Some of the clinical material for the data for this discussion is taken from the cases in the service of Dr. Harry C. Deaver, at the Mary J. Drexel Home of Philadelphia. I take pleasure in acknowledging this courtesy.

and constipation. The onset is sudden, usually when the child is a week or ten days old, although it may not appear until a month or more after birth. This, however, is rare.

At first vomiting may be irregular without any definite relation to feedings, but soon it occurs from fifteen to thirty minutes after each feeding, which is given up entirely unchanged. The gastric tolerance becomes accentuated, but as the disease progresses the vomiting becomes less frequent but more copious, that is, it is cumulative as well as projectile. One or two feedings may be tolerated, but the next will be followed by vomiting of the collected feedings. In these cases the vomitus sometimes contains well-formed clots, indicating some retention. In addition to the milk the vomitus sometimes contains a colorless stringy fluid, evidently saliva that has been swallowed, or the result of hypersecretion of esophageal or gastric glands. Blood or bile in the vomitus is very rare. The bowels are constipated, become less frequent, and the stools may take on the character of meconium. The character of the stools may be taken as an indication of the amount of food that is passing through the pylorus. Owing to lack of absorption the child is constantly hungry, the bowels are constipated, and emaciation and loss of weight are rapid.

Physical examination at this time shows the abdomen to be tense with a marked rounded prominence at the epigastrium, and resistance to palpation, sometimes also rigidity. Peristaltic waves across the abdomen are more or less pronounced, but not painful. Peristaltic waves, however, are not always present. We recently had a case under our care in which the waves could not be observed either by ourselves or by the pediatrician who referred the child to us.

According to some authorities visible peristalsis is a late symptom, not appearing until emaciation of the stomach walls sets in. The waves usually begin below the left costal margin, extending toward the median line and to the right hypochondrium beyond the region of the pylorus. According to Holt a palpable tumor is present in 75 per cent. of the cases. Downes, on the other hand, was able to demonstrate the tumor in prac-

tically all of his recent cases, and verified it at operation. He claims that palpation of the tumor is a matter of experience. When present, the tumor can be described as a round or cylindric mass which rolls under the fingers, generally located from 1 to 2 cm. to the right and above the umbilicus. In some instances, according to Péhu and Pinel, although clinically absent, the hypertrophy of the pylorus will be demonstrable at operation, and conversely, a tumor may be manifest clinically and the pylorus appear unchanged at operation. The absence of a tumor, therefore, need not exclude the diagnosis of congenital hypertrophic pyloric stenosis. Personally we find the tumor present in about 75 per cent. of the cases. In some instances we have not been able to palpate it even with the child under an anesthetic.

Patency of the pylorus is today usually determined by fluoroscopic examination. But this test is not always practicable, since the child is apt to vomit the barium meal. When feasible, however, the method is a useful guide to diagnosis and to the question of operation. Normally the infantile stomach empties itself in about three hours, so that retention at the end of four hours of 25 per cent. of the barium meal clinches the diagnosis and may be taken to indicate the necessity of surgical interference. Strauss (personal communication) lays great stress on the fluoroscopic examination. In this way he differentiates between pylorospasm and congenital pyloric stenosis, which he also believes have no connection with each other. Many of the cases of vomiting within a few days after birth he finds are instance of hyperistalsis of the entire gastro-intestinal tract, that is, a spastic condition of the tract. These cases will get well without operation, although the condition may persist for six or eight weeks.

**Treatment.**—The consensus of opinion today is toward surgical treatment of this condition, although there are a few authorities who think it can be relieved medically. Prominent among these is Haas.<sup>1</sup> He believes the stenosis to be only an advanced degree of pylorospasm—the manifestation of a general

<sup>1</sup> Jour. Amer. Med. Assoc., lxxix, 13, 14.

hypertonus due to overaction of the vagus portion of the autonomic nervous system, and that the pylorospasm can be controlled by atropin, usually 1/1000 gr. with each feeding, given until the desired physiologic effect is obtained. This may take from two weeks to several months and sometimes may require the better part of a year! In advanced cases fluid is supplied by subcutaneous administration of saline solution at frequent intervals until the child is able to take enough fluid by mouth. In this connection it may be well to remember that Thomson quotes Hutchinson as saying that "the disease is self-limited, in the sense that the pyloric lumen will eventually open up spontaneously and the child recover completely, provided he does not die in the process."

No doubt there are some cases of mild pyloric stenosis which will recover under medical treatment, but the severe cases will almost surely "die in the process" unless operated upon.

Medical treatment is usually tried out for several weeks, consisting of atropin 1/1000 to 1/70 gr. with each feeding, and thick gruel feedings. But if there is no response within a reasonable time, surgery should be resorted to. Not infrequently under this plan of medical treatment the cases are brought to the surgeon in a state of dehydration and acidosis, altogether in a desperate condition. Preliminary treatment is often necessary. This consists of soda and glucose per bowel and intraperitoneal salt solution, especially where acidosis is marked, until the child has been brought to a state where operation may be undertaken with reasonable assurance of success. Downes believes intraperitoneal salt solution as a preoperative measure favors operative bleeding, especially in older children, but we have not been convinced of this fact. Strauss (personal communication) attributes much of his remarkably low mortality not only to his especially devised pyloroplasty but also to the preoperative administration of a small blood transfusion (50 or 75 c.c.) into the superior longitudinal sinus, using a direct syringe method with a special needle. He also does not hesitate to resort to blood transfusion after operation when indicated.

According to Downes, prognosis is more unfavorable in babies

weighing less than 7 pounds. We have recently operated on a child weighing only 4 pounds, 10 ounces, with complete recovery.

Operation having been decided upon, the question of anesthesia is of first importance. In my experience a general anesthetic—ether (1 or 2 drams) is preferable to local anesthesia, the disadvantage of the latter being that the straining and crying of the child may cause evisceration, and thus make it difficult to sew up the wound.

Surgical treatment it seems was not attempted until 1893, when Cordua reported doing a gastro-enterostomy; five years later Meltzer tried the same operation; both lost their patients. Other methods were divulsion, practised by Nicoll in 1900, with success, and pyloroplasty by Braun. His patient died. Gastro-enterostomy, with an average mortality of 50 per cent., remained the operation of choice until, with the introduction of the Fredet-Rammstedt operation in 1912, surgery for infantile, hypertrophic pyloric stenosis received its greatest impetus and the mortality was gradually reduced to its present-day favorable status.

Historically, priority belongs to Fredet, as pointed out by Downes, who in 1908 was the first to suggest longitudinal incision of the serous and muscular coats of the pylorus and converting the longitudinal incision into a transverse one by suture. Rammstedt adopted the longitudinal incision, but instead of suturing, he allowed the pyloric wound to remain gaping, and it is this modification that distinguishes the operation which bears his name, and which has today become the procedure of choice. More recently Strauss, of Chicago, has devised a pyloroplasty which in his hands is giving great success. He transforms the pathologic pylorus into a normal one by unfolding the infolded mucosa, by partially shelling it out, and reducing the muscle tumor by using it as a plastic flap, which he sutures over the shelled-out mucosa. The advantage of the operation, according to Strauss, is that the shelling out of the mucosa provides immediately a free passage for the food, there is no vomiting, and improvement is rapid. The disadvantage of the Strauss operation, as we view it, is the length of time consumed for its

performance' and the extensive dissection required adds to the danger of hemorrhage.

The Rammstedt operation is, as we have said, the one most in vogue at this time. An upper right rectus incision is made from 8 to 12 cm. in length. The pylorus is brought up into the wound and with the left hand the pyloric obstruction is held between the thumb and index-finger, and a longitudinal incision is made through the peritoneal coat along an avascular line, and as one gets out into the pyloric end the dissection is continued either with the handle of the scalpel or with a blunt dissector, down until the mucous membrane presents. The tumor ends rather abruptly at the duodenal end, and particular care is necessary to avoid nicking the duodenum. If this accident occurs, it should immediately be repaired and the site covered with omental graft. The muscle-fibers at the duodenal end can be separated either with forceps (Downes) or can be stretched apart with the fingers (Strauss). Particular attention must be paid to the two small arteries, one at the gastric and one at the duodenal end, which sometimes bleed freely. They can be grasped with mosquito forceps and ligated or can be transixed and ligated. After all bleeding has been controlled, and not until then, the pylorus is dropped back into the abdomen and the incision closed in layers without drainage. Where haste is desirable the wound can be closed with interrupted sutures which should not be taken out until the tenth or twelfth day. The operation takes from ten to fifteen minutes, is attended with a minimum of shock, and convalescence is generally uncomplicated provided proper attention is paid to postoperative care.

This consists in maintaining the body heat by means of hot-water bottles, and the administration of stimulants when indicated. Postoperative vomiting may continue for a day or two. This is not due to faulty operation, that is, failure to remove the constriction, but to the preoperative general congestion of the gastric mucosa, the cause of the spasm and violent contractions. As soon as the consequent swelling subsides the vomiting also subsides. If the postoperative vomiting is severe it can usually



Fig. 140.—A, Hypertrophic stenosis; B, incising peritoneal and hypertrophic muscular tissue.

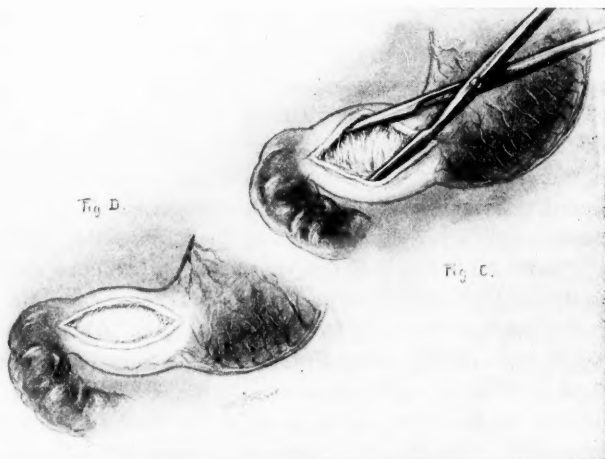


Fig. 141.—C, Separating hypertrophic muscular coat; D, operation complete, mucous membrane presenting.

be relieved by gastric lavage. Feedings can be resumed almost as soon as the infant comes out of the anesthetic. Breast milk diluted is, of course, the most desirable. Artificial feeding sometimes taxes the ingenuity of the most expert pediatrician. As a rule a low-fat formula, in small doses, 1 or 2 teaspoonfuls every two hours, with a small quantity of water between feedings is well tolerated by the little patient. Protein milk or condensed milk have also proved useful. The amount is gradually increased until the child is receiving 2 to 3 ounces of milk every three hours interspersed with water. Breast feedings also should at first be small and gradually increased until at the end of four to seven days the child is receiving the normal amount. In case not enough fluid is being taken this can be supplied by intraperitoneal saline given slowly or proctoclysis or hypodermoclysis of normal saline or soda bicarbonate and glucose for the first few days. If bowel movements have not set in within twenty-four hours, a glycerin suppository or enema or even a small suitable dose of castor-oil can be given. The child usually gains weight gradually and the stools gradually recover their normal appearance. Most cases are discharged within twelve to twenty days after operation. Breast-fed infants can be discharged sooner since the question of proper formulas is eliminated. Postoperative pneumonia was conspicuously absent in all our cases.

Much has been said and written as to the mortality of operation. This, of course, is much influenced by the preoperative duration of the illness and the kind of preoperative as well as postoperative care. Cases that are brought to the surgeon early practically all recover. This is well illustrated by the fact that Deaver in 18 consecutive cases had 100 per cent. recoveries. The average mortality of collected statistics ranges between 12 and 13 per cent. for the Rammstedt operation. Prognosis also is influenced to some degree by the weight of the child, although, as already indicated, there are exceptions to this item. As a rule a loss of more than one-third the normal for the child's age darkens prognosis, as do also poor circulation and the low alkaline reserve resulting from the more or less prolonged starvation. It is for these reasons that early operation is desirable. The prog-



nosis, however, is not in any way affected by the age of the child, nor the degree or type of vomiting, nor the presence or absence of a palpable tumor. It cannot be too often repeated, late diagnosis and late operation add to the mortality; and that it is only when all cases will be presented early that we can look for a decrease in the death-rate.

In the series of Rammstedt operations performed by myself at St. Christopher's Hospital, and by Deaver at the Mary J. Drexel Home, the operative mortality equalled about 9+ per cent. (107 cases—10 deaths). The cause of death in the series in one instance was due to peritonitis as a result of opening the duodenum; two died of hemorrhage; one of convulsions probably due to acidosis, and one of gastro-enteritis. The remaining 5 cases came to operation almost moribund, markedly dehydrated and emaciated. Death occurred from a few hours to thirty-six hours after operation in spite of all treatment and these were also probably cases of acidosis.

Pathologically these cases of infantile hypertrophic stenosis show a simple hypertrophy of the circular muscle layer, with an increase not so much in the size as in the number of fibers. Sometimes also there is an increase in the longitudinal fibers. The stomach may or may not be dilated. Wollstein, in his post-mortem study of the hypertrophic pylorus of infants dying before or soon after operation, found the stomach dilated in all instances, sometimes measuring twice the normal. The pylorus itself was also increased in size and was abnormally hard and thick to the touch. He finds this thickening to be due to an increase in the width of the circular muscle coat, the connective tissue remaining unchanged. Wollstein also studied the process of the healing of the wound after the Fredet-Rammstedt operation. This is brought about by the connective tissue of the serous and the submucous coats, the unstriped muscle cells of the cut muscle layers taking no part in the process. A thin layer of granulation covers the edges of the cut muscle and the layer of submucosa which protrudes into the gap. By the ninth day this granulation has been replaced by cellular fibrous connective tissue, and it is by the contraction of the latter and the relaxation

of the unstriated muscle that the edges of the wound are gradually approximated and the pylorus becomes relaxed. Complete healing of the wound takes place in from nine to thirteen days, although the site of the incision is still somewhat depressed. It takes about fifteen days additional for this depression to be obliterated, and at the end of about six weeks there remains only a delicate scar, which gradually also fades out, so that at the end of two years it is scarcely visible. Within two weeks after operation the pylorus is much softer than before operation, and at the end of twenty-five days has almost resumed its normal soft consistency.

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## CLINIC OF DR. RUSSELL S. BOLES

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### A CONSIDERATION OF INTESTINAL TOXEMIA WITH ESPECIAL REFERENCE TO THE USE OF COLONIC IRRIGATIONS

SINCE the time of Hippocrates evidence of a recognition of the necessity of securing regular and complete fecal evacuation has been apparent. The most primitive peoples have realized that faulty elimination is attended with misery of no uncommon sort. The present abuse of laxatives, which is appalling when the adult consumption is appreciated, is obviously due to man's instinctive effort to keep well.

The colon, serving as a receptacle for the temporary storage of fecal material, was a thoughtful provision on nature's part; and were it permitted to function as designed, there unquestionably would be an inestimable alleviation of the ills that human flesh is heir to, many of which have been proved to be due to the condition we call intestinal toxemia. As a result of disturbed function, however, stasis and toxemia occur, both of which contribute to the causation of disease.

Aaron<sup>1</sup> defines intestinal toxemia as a form of blood-poisoning induced by the absorption of toxins or micro-organisms from a damaged intestinal mucous membrane. Clinical evidence in abundance may be secured from a sober review of the subject to justify the assurance that toxemia of a severe degree can arise in the colon. Complete proof that certain toxins are formed in the colon and cause definite diseased conditions, it must be admitted, is wanting, but because we have failed to isolate such toxins it serves no useful purpose to say that there is no such thing as intestinal toxemia. Alvarez<sup>2</sup> maintains that such

so-called toxemia is a symptom-complex due to overdistention of the colon and to pressure within this viscus. It is an undeniable fact that many individuals suffer from an omission of their daily movement, but securing that movement does not always, *ipso facto*, immediately relieve them of their suffering; and this is particularly so if the omission is of frequent or steady occurrence. The preponderance of opinion favors the explanation that the symptoms observed are of toxic origin, and that persistent intelligent effort toward eradicating the toxemia is required if such symptoms are to be eliminated.

There appears to have been no satisfactory explanation of the nature of intestinal toxemia until the time of Bouchard and Metchnikoff, both of whom focused attention on what they termed "auto-intoxication." As a result of their pioneer efforts a sound scientific basis for further investigation was established. Kendall<sup>3</sup> says that the normal intestinal flora may be regarded as parasites that under certain circumstances give rise to endogenous infections. He further observes that the most important normal factor in determining the intestinal flora in health is the chemical composition of the ingested food. The ingestion of animal proteins favors the growth of the proteolytic or putrefactive bacteria, while the ingestion of carbohydrates favors the growth of the fermentative or aciduric bacteria. Levin and others have shown that certain animals, as, for instance, polar bears, maintain good health although the contents of the intestinal tract is practically sterile. The meconium of the fetus at birth is sterile, and bacteria first appear twenty-four hours after birth. After the ingestion of breast milk there is established a characteristic intestinal flora made up particularly of aciduric bacteria, among which the *Bacillus bifidus* and the *B. acidophilus* predominate. Donnelly<sup>4</sup> claims that the absence of acid-forming bacteria in the large intestine of young people is more common than has been thought heretofore, and probably accounts for many cases of severe intestinal toxemia in children. As time goes on, in direct proportion in which the animal proteins are added to the diet, the aciduric bacteria diminish and the proteolytic increase. From

a pathologic standpoint the most important bacterial action is that which takes place on protein through the proteolytic bacteria. MacLeod<sup>5</sup> states that if bacterial growth is excessive, or if there is an insufficiency of carbohydrates in the intestine, bacteria attack the amino-acids produced by the digestive enzymes and decompose them to products that may be toxic if absorbed into the blood.

Eustis<sup>6</sup> observes that the majority of these toxic substances are basic amines, such as indol, cadaverin, histamin, etc., which are formed from the putrefaction of amino-acids, which are the end-products of digestion, with loss of carbon dioxid. He states that these basic amines have a definite physiologic action, and when they are not detoxicated this action is exerted on the individual. It has been experimentally proved that they produce degenerative changes in bodily tissues, induce alterations in the blood-pressure, cause headache, vertigo, nausea, and vomiting, and have definite effects on the salivary secretions. Herter<sup>7</sup> has conclusively demonstrated the value of patient and intelligent study of the bacteria in the intestinal tract.

The x-ray studies of Cannon, Case,<sup>8</sup> Hurst,<sup>9</sup> Jordan,<sup>10</sup> and others have acquainted us with the functioning of the colon in health and disease. Case, for instance, has demonstrated that obstruction or stasis in the distal colon leads to spasm and constriction there, which is the cause of dilatation in the proximal colon. Cannon has shown us that at the junction of the distal third and the proximal two-thirds of the transverse colon there is situated a ring at which antiperistaltic waves begin, and these propel the contents of the transverse colon back toward the cecum. These phenomena are active agents in the production of cecal stasis and regurgitation into the ileum, with consequent incompetency of the ileocecal valve. Jordan, in his recent elaborate x-ray studies of the colon, has graphically demonstrated many of the functional and organic conditions that result from stasis.

Modern bacteriology, biochemistry, and the x-rays are therefore constantly opening new avenues of investigation. By correlating the results of these various lines of study we can

reasonably hope that the day will soon dawn when intestinal stasis and its resulting toxemia may be explained in a manner which will satisfy the most skeptical.

Bassler classifies the chronic intestinal toxemias as primary and secondary. He believes that in the primary cases a biochemical change from normal digestion in the intestinal canal takes place which is entirely bacterial in nature. In the secondary cases he believes that kinks, adhesions, constipation, neglected routine of life, etc., conspire to produce a toxemia which is part of a mixed infection.

Satterlee<sup>11</sup> admits that chronic intestinal toxemia is a definite entity, and is the primary cause of the protean symptoms characteristic of chronic intestinal disease. He believes that the local bacterial foci of the intestinal wall are the most important sources of infection. He reports that 150 segments of colon tissue removed at operation showed characteristic severe alterations in the structure of the bowel, particularly of the epithelium. These alterations of vital tissue, amounting in some cases to complete destruction, form a logical portal of entry for streptococci and other organisms. Friedenwald<sup>12</sup> states that the factors producing toxemia are bacterial invasion, alteration in the motility of the bowel, disturbances of the innervation of the bowel, of the endocrine system, and of the intestinal secretions, with the production of various lesions in the bowel. "It seems as yet impossible," he writes, "to determine which of these factors plays the most important part." Undoubtedly in the primary cases bacterial invasion assumes a conspicuous rôle, and in the secondary cases there must have been a primary bacterial invasion of the intestinal contents and later of the intestinal wall, lymphatics, and adjacent tissues that has led to many of the adhesions, kinks, and subsequent invasions of the appendix, gall-bladder, stomach, duodenum, etc., found in these cases. Lane<sup>13</sup> thinks the profession is just beginning to realize the enormous part played by defective functioning of the gastro-intestinal tract which leads to fouling of the food supply and consequent infection and deterioration of the tissues from absorption of septic material. This deterioration of the tissues

leads to the formation of kinks, bands, and adhesions, such as he has so graphically described, which are found, for instance, at the end of the ileum. Norman<sup>14</sup> and Eggston<sup>15</sup> are of a similar opinion when they state that it appears that gall-tract infection, pancreatitis, appendicitis, hemorrhoids, and fistulas are only localized structural manifestations of intestinal infection. If we stop to consider how frequently infection in the upper respiratory and digestive tract is associated with infection in the lower digestive tract, especially the colon, gall-bladder, and appendix, it is not surprising that complete relief is not afforded patients who have had the former infections removed and the latter neglected. Slesinger<sup>16</sup> asserts that as a result of continuous stasis, which occurs in the different portions of the colon, new bands of tissue in the mesenteries of the portions affected (*i. e.*, pelvic colon, splenic flexure, hepatic flexure, and ileocecal region) appear, and that these bands tend to produce kinks, adhesions, and secondary changes in other organs.

Under normal conditions bacteria such as inhabit the intestinal tract would probably exert no deleterious effect on the human organism. Normal conditions in the colon are, however, unusual. Stasis is the rule, and infection develops as a result of stasis. Long-continued infection eventually leads to degenerative changes in the liver, pancreas, and other organs. Inasmuch as the liver is the most powerful detoxifying organ in the body it is inevitable that, in time, it should fail in this function, and when this occurs systemic conditions are to be expected. Were it not for the development of intestinal stasis, certain strains of bacteria—the colon bacillus for instance—might even exert some protective influence in the tract, but given opportunity for their full development infections in most cases may be expected to result.

#### SYMPTOMATOLOGY

As the symptoms and physical disabilities resulting from intestinal toxemia are so varied and numerous we shall direct attention only to those that are of particular significance or of unusual occurrence. Among the more pronounced general

symptoms one encounters fatigue, mental or physical depression, anorexia, flatulence, vertigo, *muscae volitantes*, headache, particularly occipital headache, a tenseness and drawing sensation in the back of the neck, cold extremities, and various paresthesias. It is quite probable that certain intestinal toxins have an affinity for certain tissues, and as a result one class of patients may present mental, another nervous, and still another gastro-intestinal manifestations.

Of the more important gastro-intestinal symptoms, those simulating ulcer are frequent, and obviously demand careful analysis. It is no unusual occurrence to have patients present themselves with a previously made diagnosis of gastric ulcer, and to find that their symptoms are entirely relieved by treatment of the intestinal stasis which is usually present. A prominent roentgenologist remarked to the author that he thinks he sees fewer and fewer gastric ulcers. They probably occur much less frequently than most of us suppose. Anorexia and fulness and distention after eating are usually associated with intestinal toxemia. The foregoing symptoms may be due to disturbances of secretion or motility, such as hyperacidity or achylia, and atony or pylorospasm and enterospasm are known to occur as a result of intestinal toxemia. Absence of gastro-intestinal symptoms may be misleading, and, as Satterlee<sup>17</sup> states, "one of the most puzzling aspects of gastro-intestinal infection is that it may produce profound mental or nervous disturbance with little or no definite gastro-intestinal symptomatology."

Nervous and mental symptoms are frequently encountered. Twitching, especially of the eyelids and lips, paresthesias, mental depression, melancholia, and conditions simulating epilepsy and dementia præcox are not uncommonly observed. Cotton<sup>18</sup> is of the opinion that there would be a great diminution in the number of patients with mental symptoms were their foci of infection eradicated; and this applies especially to infection in the colon. Stockton<sup>19</sup> says that "long continuance of infection of the digestive tract, inducing a lowering of the general nutrition, leads to depression or irritation of nerve tissue, and sometimes appears to be the exciting cause of brain disease and



also an aid to its continuance." This author insists that a careful study should be made of the character of the intestinal flora, particularly that of the colon. He has noted that a remarkable improvement follows in patients who are deprived of foods containing animal proteins and also after deliberate attempts are made to change the intestinal flora, especially those involved in the putrefactive alterations of the animal proteins and the incidental production of toxic substances.

Anemia, in the author's experience, is the rule in intestinal stasis. Usually there is found a diminution of the hemoglobin to the extent of 70 or 80 per cent. Herter<sup>20</sup> notices changes in the morphology of the red cells characteristic of primary pernicious anemia in 9 cases of infection of the intestinal tract with *Bacillus welchii*. He also makes the interesting observation that carnivorous animals frequently suffer from pernicious and other types of anemia, while herbivorous animals rarely have these diseases unless they are due to intestinal parasites.

Cutaneous lesions that have been rebellious to other forms of treatment frequently heal when intestinal stasis and toxemia are eliminated. Acne, eczema, erythema multiforme, erythema nodosum, and urticaria it appears often owe their origin to an intestinal focus of infection. The author has observed that ridging and brittleness of the nails and loss of hair commonly occurs. He has had 3 cases of dystrophia unguum which cleared up under treatment for intestinal toxemia. No reference has been found in the literature on the association of this condition with intestinal toxemia. The skin is often dry, wrinkled, and of a dirty, sallow hue, presenting areas of brownish pigmentation, especially on the abdomen and under the eyes. Erythema of the hypothenar eminences has frequently been observed by the author. Endocrine disorders can at times be traced to intestinal toxemia. Hyperthyroidism and hypothyroidism, simple enlargement of the thyroid, and adrenal insufficiency are thus explained by some authorities. Mastitis, as Jordan has observed, is also a frequent development.

Ocular symptoms, such as burning and aching of the eyeballs, muscæ volitantes, and blurring of the vision which may be

due to retinal deposits frequently occur. Some cases of iritis, choroiditis, and corneal ulcer have been known to improve after the eradication of intestinal toxemia. The author has under treatment a patient who suffers from attacks of the most intense conjunctival hyperemia each time he permits intestinal stasis to develop.

#### DIAGNOSIS

As many of the foregoing symptoms may develop in the course of other conditions, a close analysis of the symptoms and a careful physical examination are required before a diagnosis of intestinal toxemia should be made. *x*-Ray examination of the intestinal tract is always advisable. The carmin test is helpful in determining whether stasis exists. The routine laboratory tests of the feces and urine, including a bacteriologic examination of the feces, should always be made, noting in the latter the proportion of Gram-positive and Gram-negative organisms and determining the identity of each. The character and number of stools, consistency, reaction, odor, color, and shape should be noted. The presence of blood or mucus should be determined and also the form in which the mucus appears. Search should be made for parasites and food remnants. The routine microscopic examination should be carried out. Aside from the routine examination of the urine one should determine particularly if indican is present. In testing for this substance it is advisable to examine several specimens throughout the twenty-four hours, as it frequently is found at one time of the day and not at another. When manifest intestinal toxemia of the putrefactive type is present and indican is not found, it probably indicates, according to Norman, that the ileocecal valve is competent and is preventing a regurgitation of large numbers of colon bacilli into the small intestine where their action on a relatively free carbohydrate medium produces indol. Other factors of safety, such as a normally functioning liver which destroys the indol, must be kept in mind. In the process of detoxifying aromatic toxins which must rationally arise from the intestinal contents, the central cells of the liver lobules are prone to injury according to Whipple and Sperry. Eustis has demon-

strated that there is a synchronous rise and fall of the percentage of indican in the urine with a rise and fall of the intensity of Ehrlich's aldehyd reaction. Conceding that the latter test gives valuable information as to the functional capacity of the liver, this finding suggests that liver function may be disturbed as a result of continued production of indol in the intestines.

Wilson found indican and acetone in 36 individuals whose intake of protein was high; in all these cases albumin and sugar were absent. In the author's experience, however, albumin or sugar in the urine is not uncommonly detected in association with an indolic type of intestinal putrefaction. In such cases the albumin or sugar disappears with the eradication of the intestinal putrefaction. Regarding this phenomena Eustis says, "In the process of detoxicating aromatic poisons the liver utilizes sulphuric acid and acetic acid. In certain cases where there is excessive absorption glucose is partially oxidized to glycuronic acid and the toxins are excreted as combined glycuronates. Urines containing these combined glycuronates will reduce alkaline copper sulphate solutions." Bassler lays great stress on the value of indol and acetic acids in the estimation of solids and phosphates, and in the quantitative estimation of sulphates, urea, uric acid, oxalic acid, ammonia, and bile-pigments. While the presence of an excessive amount of indican in the urine is a help in establishing the diagnosis, probably the best single index of the degree of intestinal putrefaction is afforded by the determination of the ethereal sulphates, which, however, does not aid in determining the character of the putrefactive products.

In this connection it is worth bearing in mind the possible association between certain cases of uremia and intestinal putrefaction. As a result of the work of Nellis B. Foster, Eustis<sup>21</sup> remarks that any amines of intestinal origin if in the circulation, would increase the percentage of undetermined non-protein nitrogen of the blood. It has been shown that this so-called rest nitrogen is greatly increased in the convulsive type of uremia. Indican has been demonstrated to be increased in uremia, rising from the normal 0.05 to as high as 2.2 mg., and, as Eustis says,

"While it is not claimed that uremia is due solely to the absorption of intestinal toxins, there is enough evidence at hand to warrant a consideration of these toxins as an important factor in the symptom-complex of uremia, and to warrant the daily examination of the urine for indican, and a diet in the nephritic which will not putrefy in the intestines."

#### TREATMENT

In the treatment of intestinal toxemia naturally our first effort must be directed to correcting intestinal stasis and alleviating the catarrhal processes resulting from mechanical or inflammatory lesions of the gastro-intestinal tract. The operative treatment will not be discussed.

Diet is of paramount importance. It is essential that a well-balanced ration containing a sufficiency of minerals, and a proper variety of vitamins, such as are found in fresh green vegetables, fruits, milk, cream, butter, egg-yolk, bran, beans, beef, and other fresh meats, cereals, etc., be administered. Consideration should be given to the proper preparation and cooking of foods. Locke,<sup>22</sup> for instance, shows that when meats are boiled as much as 12 per cent. of the protein, 37 per cent. of the fat, and 67 per cent. of the salts are found in the broth. When meats are roasted as much as 4 per cent. of the protein, 57 per cent. of the fat, and 57 per cent. of the mineral salts are found in the drippings. Vegetables undergo a similar loss when submitted to the process of cooking, for instance, as much as 58 per cent. of the nitrogenous matter and 38 per cent. of the mineral matter is lost from potatoes that are boiled without the skins.

The type of toxemia with which we are dealing must determine the character of the diet prescribed. It is necessary in the putrefactive or indolic form of toxemia to restrict greatly animal proteins such as are found in meat, fish, eggs, and cheese, and to supply the body with less readily decomposed vegetable proteins such as are contained in fruits and fresh green vegetables, both of which should be used abundantly. Well-cooked cereals served with milk-sugar, whole wheat bread, butter,

olive oil, salads, and plain desserts, such as gelatin and custard, are valuable accessories to the dietary. If, on the other hand, we are treating a patient with the fermentative type of toxemia, a high percentage of animal protein such as is found in beef, lamb, chicken, fish, and eggs is indicated. In either case highly refined foods should be interdicted, and water should be taken abundantly between meals. Other beverages which have proved to be beneficial are buttermilk and acidophilus milk.

Another essential point to which Weinstein<sup>23</sup> calls attention is the fact that in intestinal stasis the load gravitating on the colon is too big, and that it is, therefore, important to lighten this burden by reducing the quantity of food ingested at one time.

Substantial clinical evidence has been gathered to make it appear that in patients suffering from intestinal toxemia much may be expected in the way of improvement from the use of vaccines and acid-producing bacteria such as the *Bacillus acidophilus*. Bassler believes the best results from bacterial treatment accrue from the use of autogenous vaccines. From the study of a large group of cases he claims to have had excellent results from injecting into the rectum viable non-toxic strains of the infecting organism. Although the author's experience with Bassler's method has been somewhat limited, the results thus far have been gratifying. Norman and others claim good results from autogenous vaccines prepared from cultures taken from drainage of the colon combined with cultures from such other foci of infection as may be found in the teeth, tonsils, etc. Torrey and Rahe<sup>24</sup> have demonstrated from experiments on dogs that by the use of autogenous vaccines it is possible to produce at least a temporary suppression of corresponding strains of *B. coli* naturally vegetating in the digestive tract. If the strain of *B. coli* giving rise to the toxic products could be determined, which, however, is exceedingly difficult, the incorporation of these strains in an autogenous vaccine should be very helpful. Vaccine therapy may be expected to produce the best results in those cases which present definite and especially severe symptoms of intestinal toxemia, where the exciting infection is prob-

ably present in the mucosa to a greater extent than in the intestinal contents.

*Bacillus acidophilus* should theoretically be of great help in correcting intestinal stasis and toxemia, since it is an active producer of lactic acid and can be successfully implanted in the intestine, as has been shown by Rettger, Cheplin,<sup>25</sup> and others; there is much substantial clinical evidence that can be adduced in support of this theory. It is, however, important to administer such special diets as favor this implantation. It has been shown that 1000 c.c. of active milk culture of *B. acidophilus* will effect a transformation of the intestinal flora in a few days, and the same result may be obtained by giving one-half the amount of such a culture reinforced with 100 grams of lactose. The acidophilus organism can be effectively administered in milk, whey, or beef-broth culture. Tablets of this organism are valueless, however, owing to the small numbers of active bacilli they contain. From an extensive use of the *B. acidophilus* the author's studies show that when the stool is alkaline and contains a little gas and an excess of *B. coli*, the implantation will not take place, or if it does take place it will be slight and only temporary. Individuals with normal groupings of bacteria or acid-forming bacteria will show a good implantation.

**Colonic Irrigation.**—From a very extensive use of colonic irrigation and a close observation of the results following its employment the author is firmly convinced that this procedure is of great value in relieving the symptoms of intestinal toxemia. This method of treatment first came into vogue at Plombières, France, in the time of Napoleon III. It has commended itself for many years, and, as Walker and Lewis<sup>26</sup> say, "There is no doubt that good results follow its practice." Gant<sup>27</sup> observes that irrigations may be employed principally for healing local lesions of the mucosa and cleansing the bowel of toxic or putrefying foods. He says that experience has demonstrated that small cool high or low enemas may be resorted to for a long time and do but little harm. He believes that the best results in obstinate or habitual costiveness are obtained from the use of a daily injection of 1 to 3 pints of cold water at 70° to 80° F.

He states that the cold enteroclysis appears to benefit the whole body, especially the gastro-intestinal tract; that it not only acts as an irrigant and solvent, but as a powerful tonic, which increases peristalsis, causes the glands to secrete more mucus, lubricates the bowel, augments circulation, and diminishes auto-intoxication through stimulation of the skin, kidneys, and liver. By means of hot-water enteroclysis he believes he has relieved many patients suffering from flatus, colic, rectal tenesmus, hemorrhoids, etc.; he attributes the beneficent action of the water to the high temperature which has a soothing effect on the bowel causing the fibers to relax and permitting the feces to pass. It is well to bear in mind, however, that copious injections are contraindicated in patients suffering from phthisis, arteriosclerosis, dilatation of the heart, and ulceration or dilatation of the colon.

Inasmuch as many different methods for giving a colonic irrigation have been in vogue, the author has made a special effort to work out a satisfactory technic. With some modifications the technic practised by the late Dr. Charles Seltzer appears to give the best results. The fact that with this method the entire colon up to and including the cecum is cleansed has been verified by Dr. Ralph Bromer and the author by means of roentgenograms which were obtained after a mucilage of acacia suspension of barium sulphate in water was used to irrigate the colon.

The apparatus employed consists of a 3-gallon glass irrigating jar to which is connected a Valentine tube. The distal end of the Valentine tube is connected with a T-glass connecting tube. On the opposite end of the glass tube is attached a piece of large rubber tubing, 2 feet long, on the distal end of which is the rectal tube. The rectal tube is a cylindric nickel-plated metal tube, 16 cm. long, and with a single opening 8/10 cm. in diameter at either end. To the outlet of the glass connecting tube is connected a rubber tube to carry off the drainage. The use of two tubes, two-way tubes, long colon tubes, and of rubber tubes has been found not to give the same results as the tube above described.

It is recommended that the patient be instructed to secure a movement before coming for irrigation by taking mineral oil or a small enema. In giving the treatment the patient is placed in the Sims position on an unyielding table. The rectal tube is lubricated and is inserted only a few inches. From the glass

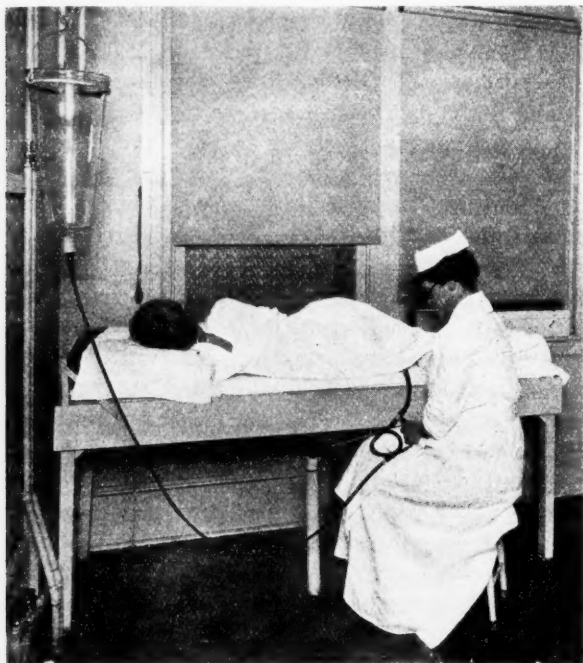


Fig. 142.—Method of giving colonic irrigation. Note position of patient. Intake and drainage controlled by nurse's hand. Unless specimen of the return is to be saved, drainage flows directly into sewer after being inspected through glass T tube.

irrigating jar, which is suspended so that the bottom is 18 inches above the table, the solution to be used is permitted to run slowly into the rectum in amounts varying from 1 to 2 pints. The inflow is then checked and the solution in the colon is drained off, its character meanwhile being observed through



the glass tube. This procedure is repeated until the drainage returns clear, which may take in all from 3 to 6 gallons of solution. If there is any distress the patient is permitted to get up and empty the colon. Care is exercised to see that the solution runs in slowly and never at one time in amounts sufficient to distend the colon or cause discomfort. It may be necessary to vary the temperature of the solution. In spastic types of colitis

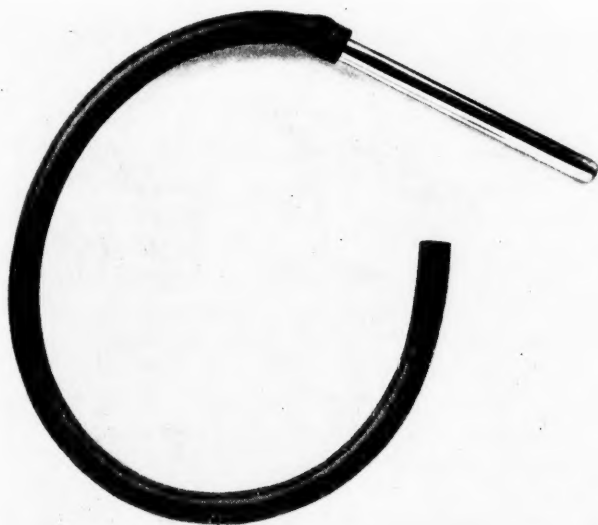


Fig. 143.—Colon tube used by the author in giving irrigations.

and in inflammatory conditions a temperature of 108° or 110° F. is advisable, while in atonic colitis cooler solutions, at about 90° F., are better tolerated. In most cases ordinary tap-water may be used, although, depending on the conditions present, normal saline, carbonate of soda, and various medicated solutions or dyes may be indicated. Crohn has recently recommended the use of neutral acriflavine solution for colonic irrigation in the treatment of chronic ulcerative colitis, and Bassler

believes that injections of gentian-violet into the colon are of value in changing the fecal flora.

Modifications of the treatment, such as changes in the position of the patient, the amount and temperature of the solution used, etc., may have to be employed to suit individual cases. Abdominal massage facilitates drainage and is usually given before and after the irrigation. In the treatment of atonic constipation the use of the faradic current applied by means of the Morse Wave Generator following the irrigation appears to be of value. A reaction of any kind during or after a skilfully administered colonic irrigation has been exceedingly rare in the author's experience.

Transduodenal lavage is helpful in the treatment of these cases, especially when iléal stasis is pronounced, or there is much regurgitation through an incompetent ileocecal valve. Einhorn describes 2 cases in which ulcerative lesions of the colon not yielding to any of the usual modes of treatment were cured by irrigating the large bowel with mercurochrome through a jointed intestinal tube which is swallowed by the patient until the end reaches the site of ulceration.

As a result of the work of Schmidt, Bouchard, Bauman, and others it appears that all so-called intestinal antiseptics are ineffectual in securing any real antiseptics in the intestine. Creosote and betanaphthol may have some antiseptic influence if (by administering them in an enteric-coated tablet) their absorption is delayed until they reach the colon. Recently dimol has been recommended as an intestinal antiseptic. Such general tonics as iron, strychnin, arsenic, and the glycerophosphates are often indicated. All laxatives have been shown to have a pernicious effect when routinely used; therefore their employment, except for an emergency or temporarily in intractable non-surgical cases, is unwarranted. Agar-agar and mineral oil may be used to great advantage in overcoming stasis. The agar-agar is given preferably in granular form, in tablespoonful doses once or twice daily. A pure mineral oil of high viscosity may be given also in tablespoonful doses two or three times a day. The separate use of these remedies seems to be more effective than administering them together in emulsion form.

In addition, such corrective measures as proper posture, abdominal exercises, and outdoor exercise are obviously important aids in the treatment. The practice of deep breathing is also beneficial. When stasis is associated with ptosis the application of properly fitting belts or corsets is necessary. The Rose moleskin belt may be used temporarily to good advantage. In some cases without ptosis the wearing of a support gives great comfort, probably because of the increased intra-abdominal pressure which is established. Detailed instructions in the adjustment of the corset should always be given the patient, emphasizing particularly the importance of applying the support while in the recumbent position.

#### SUMMARY

1. Clinical experience, together with a study of the literature, makes it evident that the condition known as intestinal toxemia actually exists, even though the toxins have not been demonstrated in the blood.

2. Intestinal stasis initiates chemical changes and bacterial decomposition in the intestinal contents, and these forces working together produce alterations in the tissues that permit the toxins generated in the intestinal tract and bacteria to invade the tissues, blood-vessels, and lymphatics, and eventually to interfere with general nutrition and to bring about degenerative changes in the liver, pancreas, and other organs.

3. The symptoms of intestinal toxemia are manifold. They may be gastro-intestinal, ocular, cutaneous, nervous, mental, etc.

4. A diagnosis of intestinal toxemia should only be made after careful physical examination and laboratory tests exclude the possibility of organic disease. The urine and feces should be submitted to careful chemical and bacteriologic tests. The aid of the x-rays should also be invoked. The presence of an excessive amount of indican in the urine is a help in establishing the diagnosis; the best single index as to the degree of intestinal putrefaction is afforded by the determination of the ethereal sulphates. This procedure, however, does not determine the character of the putrefactive products.

5. Treatment must be directed to overcoming intestinal stasis, alleviating catarrhal processes, and restoring muscular tone.

6. The character of the diet is of first importance and depends upon the type of toxemia present. In the indolic type, which is the most frequent, a low protein and high carbohydrate diet is indicated, while in the fermentative type the reverse is required.

7. Much may be expected from the proper use of vaccines (particularly autogenous vaccines) and acid-producing bacteria such as *Bacillus acidophilus*. The latter should always be administered in milk cultures, not in tablet form, combined with lactose.

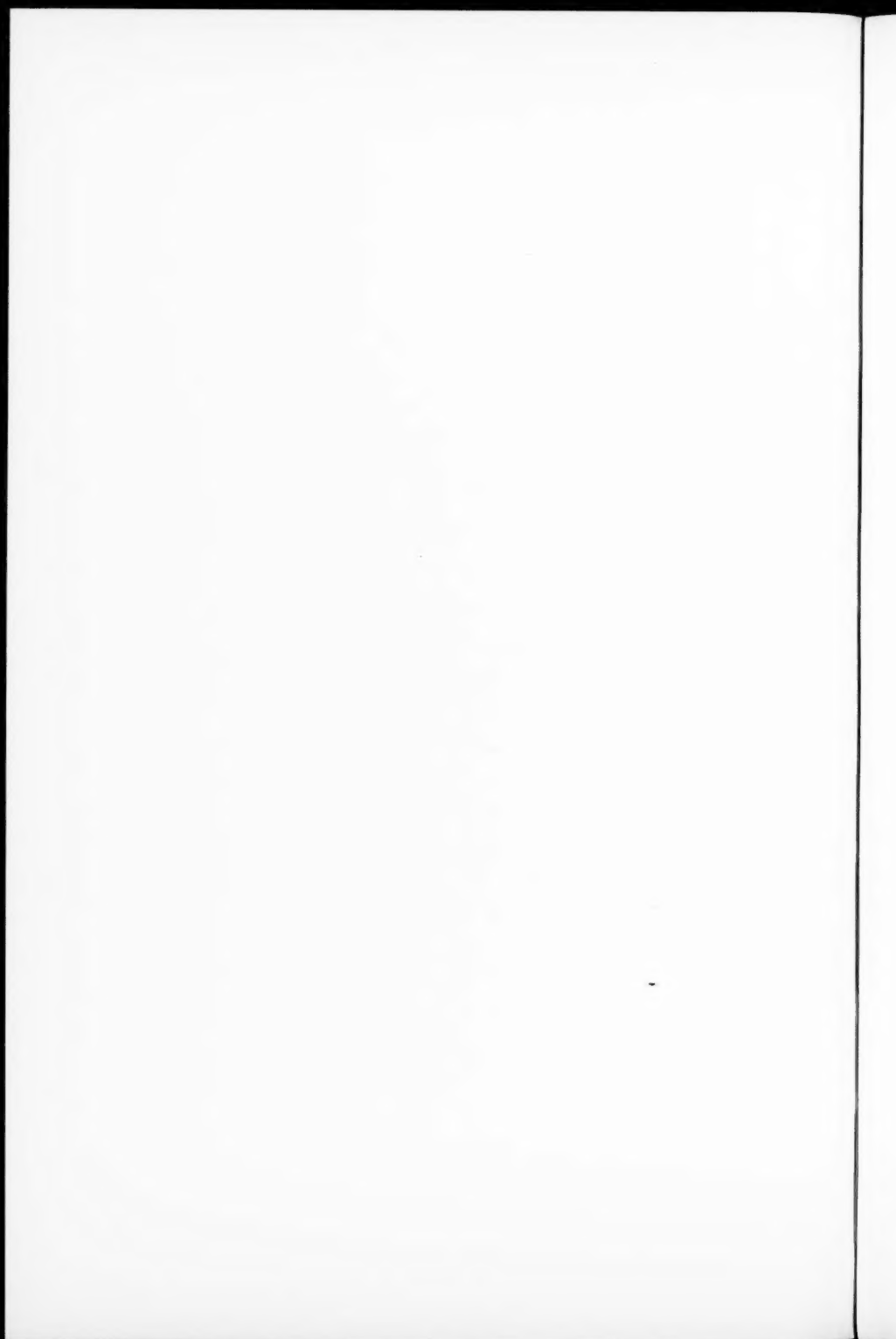
8. Colonic irrigation is a valuable adjuvant in relieving stasis and atony and their resulting symptoms. When carried out according to the method described by the author its benefits are pronounced and no deleterious effects have ever been noted.

9. Other aids in treatment are the administration of agar-agar and mineral oil, correction of faulty posture by well-adjusted corsets or belts, outdoor exercise, special exercise and massage for the abdominal muscles, and deep breathing. The application of the faradic current following irrigation appears to be of value in overcoming atonic constipation. The use of laxatives is contraindicated.

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## CLINIC OF DR. T. GRIER MILLER

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### SYPHILIS OF THE LIVER

#### **Report of a Case with Pleural Effusion in a Young Woman. Infection Probably Acquired in Childhood.**

I WISH to show you today a patient who has been under our observation irregularly for about six months and who presents the picture of syphilis localized chiefly in the liver. The interesting points in her case have been an unusual mode of infection, a sudden onset of symptoms after an abdominal operation, and a complicating pleural effusion. The latter two features in the beginning served only to confuse the diagnosis which was finally made by serologic examination and proved by the results of antisyphilitic treatment. I will give you her history as originally obtained from her and subsequently amplified by her family physician and others, and discuss the case before presenting the patient herself.

**Medical and Social History.**—G. N. B., a young woman of twenty-three years, was first in our hospital March 3 to 17, 1924, complaining chiefly of a cough and of pain and a mass in the right upper abdomen. As a child she had been considered very healthy, although she had experienced measles at eight years of age, scarlet fever and chickenpox at twelve, and some sort of a bone lesion in the right upper arm at fourteen. She had also had a number of operations: a right-sided inguinal herniorrhaphy at twelve, a tonsillectomy at fourteen, an appendectomy at seventeen, and finally a left inguinal herniorrhaphy at twenty. Her present illness clearly dated back to the time of the appendix operation in 1919. Within a few days

following that she developed for the first time severe, sharp stabbing pains in the right upper abdominal quadrant, these keeping up irregularly for two months and then disappearing completely. She was told at the time that these pains were due to adhesions.

Soon after the subsidence of the abdominal pains she herself discovered a lump where the pains had been, and she thought that it was as large then as at any subsequent time. This mass, however, caused no special discomfort, but for some months after this she was not very well. Her complaints then were, however, of a different nature. Her menstruation was irregular, she had pains in the left lower abdomen and in the lower back, and during the fall of 1919 she had pain in the lower left chest. Her physician noted that her hands and feet were at times quite reddened, especially along the edges. Then for a year or more she seemed much better. In May, 1921 she developed a cough and a pain under the left breast and râles were found at the base of the left lung.

In October, 1922, three years after the original attack, the old sharp stabbing pains in the right upper abdomen recurred and kept up intermittently. They were never present during the night, although when lying on her left side she sometimes had the sensation of something making pressure in the right abdomen. Coughing increased the pain and it radiated to the back in the right scapular region. There was some associated local tenderness.

In the meantime she had developed a left inguinal hernia, and apparently it was thought that this might be the cause of her abdominal pains. In any case a second herniorrhaphy was performed on October 27, 1922, but before leaving the hospital a marked cough developed. On returning home it was found that she was running an evening temperature of 101° to 103° F. and she was quite dyspneic. She developed signs of fluid in her right pleural cavity. A roentgenologic study confirmed this. A paracentesis thoracis was performed, 1500 c.c. of thin yellowish fluid being obtained. Subsequently for several months an aspiration had to be performed every two or three weeks. The fluid



was never purulent and became more and more clear with the repeated tapplings. The abdominal pains gradually subsided and the fever finally disappeared.

The cough had kept up during all this time, worse in the mornings, but productive of only a little frothy mucus. There was no marked chest pain, no hemoptysis, and she had no night-sweats, but there did occur a steady loss in weight, from 135 down to 111 pounds. At times she had attacks of pain over the kidney regions with extension down the backs of the legs, often one side at a time. This was always relieved by lying down and was entirely independent of the pain in her upper right abdomen.

In January of the next year the right abdominal pains reappeared for the third time, and again she had an evening fever. There was also a slight reaccumulation of fluid in the right chest. A consultant, who saw her on March 4th, made a diagnosis of sarcoma of the right kidney with metastasis to the right lung. On the following day another paracentesis was done and 1500 c.c. of fluid of the same character were secured. A roentgenogram made immediately after this showed no pulmonary lesion. Other aspirations were performed on March 23d, April 5th and 25th, about 1500 c.c. being removed each time. Then she complained of a girdle-like pain about the waist and the pain in the right upper quadrant was more marked and radiated to the epigastrium. After that no immediate return of fluid in the chest was discovered and she felt fairly well the rest of the year, her weight increasing to 139 pounds.

Then, in January, 1924, she developed what was at first taken to be a cold, had a return of the cough, fever, and abdominal pain, and again her physician discovered the signs of a right pleural effusion. The cough was not marked, but it and the fever were still present at the time of our first seeing her last March.

There had been no digestive symptoms other than constipation and some gaseous distention of the abdomen at times. Her appetite had not been specially affected. There were no cardiac, urinary, or nervous symptoms.

The patient's social history is very interesting and will be

given at this stage in the presentation, although it was not obtained in full until some weeks after the original discharge from the hospital. She was an illegitimate child and knew nothing of her father. Her mother was subsequently married, this occurring within the memory of the patient. She had one sister. At the age of eight she had been placed in the hands of another woman by her mother who was at that time leaving the city in which they had lived. This woman kept her for two years and during that time the child dressed certain discharging sores which the woman had on her face and leg. It is presumed that it was for this purpose that the child was taken by this woman, for, the patient stated, "no one else would do it." Finally some charitable organization took the child in hand and she was adopted by a minister and his wife in another part of the state. There in a small country town she has since lived under quite favorable circumstances. Her habits have been good. She has been under no physical or nervous strains of any kind.

**Physical Examination.**—Examination made at the time of her admission in March showed the patient to be an intelligent, well-developed and fairly nourished young woman of the distinctly blonde type. Some vasomotor instability was noted. She did not seem to be particularly sick or uncomfortable. Her pupils were equal, round, and reacted promptly to light and in accommodation. The teeth were in good condition, showing no defects of any kind. The tonsils were cryptic and congested, but not clearly septic. There was no evidence of thyroid pathology.

Her chest was well formed and expansion was good and equal on the two sides, but at the right base posteriorly, below the scapular angle, there was definite impairment to percussion, vocal and tactile fremitus were a little diminished, and the breath sounds were distant. The upper level of percussion impairment moved up and down with respiration. The heart was displaced to the left, the right border being at most only 1 to 2 cm. to the right of the midline. There was no cardiac enlargement, though a soft systolic blow was audible at the apex.

The abdomen was asymmetric, the right upper portion being noticeably prominent on inspection. Here an irregularly

round mass was easily palpable, this extending down well below the umbilical level, across to the midline, and then upward into the epigastrium, where the firm, rather irregular edge could be felt as it made a right-angled turn to the left and disappeared under the left costal margin. This main mass could be pushed from side to side, moved up and down with respiration, and gave the impression of having a rough, somewhat uneven surface. Passing across it transversely just below the costal margin there seemed to be a depressed groove which at first was thought to indicate that the lower mass was separate from, but in apposition with, an enlarged liver above. The spleen was moderately large and easily palpable. The only other abnormal abdominal findings consisted of three operative scars, two in the inguinal regions (hernia operations) and one in the lower right quadrant (appendectomy). The hernia had recurred on the left side and a truss was worn.

Her deep tendon reflexes were quite normal and the tests for sensation were negative.

**Special Investigations.**—There was a slight irregular fever, the temperature ranging from 97.6° to 100° F., and the pulse tended to be a little frequent, 78 to 100. Weight 123 pounds.

The urine was negative and the elimination of phenolsulphonephthalein was adequate, 65 per cent. being recovered within two hours after intravenous injection.

There was a moderate anemia of the secondary type, the red blood-cells numbering 3,800,000, and the hemoglobin reading being 63 per cent. There were 10,300 leukocytes, of which 81 per cent. were polymorphonuclears. Subsequent blood examinations on that admission showed the hemoglobin up to 80 per cent., the red cells to 4,800,000, and the leukocyte count together with the differential results normal.

A simple gastric analysis showed no free hydrochloric acid, with a total acidity of 38, while a fractional analysis later revealed that free hydrochloric acid was present in small amounts (up to 14) at certain times in the digestive cycle, the total acidity at the end of an hour reaching 47. There was no evidence of gastric retention.

A special examination of the eyes showed only very slight hyperopia. There was no keratitis.

Roentgenologic study of the chest confirmed the clinical opinion, showing only a very marked elevation of the right diaphragm. It was suggested in addition by the roentgenologist that there might be a small right-sided pleural effusion or some thickening of the basal pleura.

Because of the history of some disease of the left humerus at the age of fourteen a roentgenogram was made of this bone, but no lesion was discovered. In spite of this it was the opinion of some of the clinicians that this bone seemed a little thickened at one point.

A Wassermann test on the blood-serum was reported as strongly positive. A similar report was received on a second specimen of blood taken a few days later.

**Discussion.**—Knowing now the result of the Wassermann test one is, of course, given an immediate point of view about this case, but before that was in hand the question of a diagnosis was a most intriguing one and caused no little speculation on the part of the members of the medical staff of the hospital, who always feel it incumbent upon them to make a diagnosis before the laboratory data is obtained.

The apparent onset of the trouble within a few days of her appendectomy and the prominence of the upper right abdominal pain without any indication of chest disturbance at that time seemed to suggest that the primary lesion was below the diaphragm and possibly secondary to the operation. A suppurative pyelophlebitis was therefore considered. Such a lesion does sometimes follow this surgical procedure, and it could have accounted not only for the painful right upper abdomen but also the mass, for an enlarged sore liver is the outstanding finding in this condition. Of course we had no history of fever, chills, sweats, and prostration at that time, but, on the other hand, we did not know that they had not been present. Furthermore, chest troubles not infrequently develop secondarily to suppurative liver diseases by extension through the diaphragm. This theory, while at first thought attractive, could not be seriously

entertained because of the fact that after two months she was comparatively well again but for the large mass, and remained so for about three years, and the pleural effusion developed after that long interval. Pylephlebitis is a fatal disease unless treated surgically.

It seemed proper, therefore, to consider some upper abdominal lesion that had not such a serious immediate prognosis and that could cause a large, tender, painful mass with subsequent disappearance of the pain and soreness, but not necessarily the mass, for a long time. It even seemed possible that she might not have had an appendicitis at all, but that her original trouble, for which she was operated, was higher up, and the appendix removed in error. An acute inflammatory gall-bladder lesion was, therefore, given some thought. It was considered that such an acute lesion might have been associated with both hepatic and gall-bladder enlargement, that the acute symptoms might have spontaneously subsided, leaving some chronic condition with perhaps cystic duct obstruction, and finally the development of a Riedel lobe of the liver, that subsequently this gall-bladder infection might have been lighted up again, even after three years, and that then a subphrenic peritonitis with extension through to the pleura might have occurred. It seemed unlikely, however, that either a distended gall-bladder or a Riedel lobe could possibly have become so large as the mass which we palpated and which the patient said was just as large two months after the onset of her trouble. Furthermore, an intense jaundice would almost certainly have been present with such an affection in its early stages, and this surely would not have been forgotten by the patient or overlooked by her physician.

The long duration of the trouble and the comparatively good general condition of the patient, as well as her age, seemed to eliminate the probability of a malignant lesion, either sarcoma or carcinoma. Likewise a parasitic cyst of the liver seemed unlikely because of the patient's American origin and life, and also because only by rupturing into the pleura could such a lesion have caused the pleural effusion, and in the fluid removed in such a case daughter-cysts would probably have been seen.

Furthermore, it would have been difficult to explain the subsidence of the pain after the first two months.

Finally, syphilis was thought of, but in the absence of any stigmata of the congenital variety, of any other physical signs of that disease, and of a suggestive history (we did not know the social and family history then) this did not receive the consideration it deserved, and the diagnosis was not made. Even when the first Wassermann test was reported as positive there remained a doubt in our minds. After getting a second positive report it was deemed wise to apply the therapeutic test. This proved positive, as will soon be seen. Furthermore, we soon learned more of the history which gave support to this diagnosis.

With this etiology now established it is instructive to review the case in an effort to determine if possible the time and mode of infection and the progressive development of the pathologic lesions.

It is not possible to determine with certainty whether the disease in this instance was congenital or acquired. The mother has not yet been located, although what we know of her would suggest at least the possibility that she was syphilitic. A Wassermann test on the patient's sister was done and reported as negative. The history of a bone lesion at fourteen is suggestive of congenital syphilis when taken in conjunction with the large spleen and liver. This bone lesion is doubtful, however, in view of the negative Roentgen-ray examination. If congenital it is of the delayed type, and such cases, unlike this one, are nearly always ill-developed both physically and intellectually.

A possible source of acquired syphilis is to be thought of in connection with the woman whose facial sores the patient dressed from her eighth to tenth years. I have searched out this woman in another city and found her face covered with irregularly round patches of scar tissue, the size of a dime on the average, these being most concentrated about the central portion of the face, over the nose, the upper lip, and the anterior portions of the cheeks. They had a punched-out appearance and looked much like the scars that result from rupial syphilids. There was no positive evidence of bone or cartilaginous

destruction. When inquiry was made about these lesions she stated that they were due to an attack of erysipelas. It was not possible, unfortunately, to get a specimen of blood for a Wassermann examination. It seems to me quite probable that the patient's disease was contracted as a result of her intimate contact with this person, and therefore acquired. Under the circumstances of the patient's life at that time it is not difficult to imagine both the primary and the secondary stages being overlooked. The tertiary lesions probably developed rapidly because of the youth of the patient, although even in adults these developments sometimes occur within a few years after the primary infection.

It seems reasonable to suspect that at the time of the appendix operation the liver was already involved by syphilis, and that the trauma of the operation caused a rapid increase in the development of the disease process, with a resultant perihepatitis which caused the pain. It is well known that long remissions occur in the manifestations of this disease and so the intervals of comparatively good health can be explained. After three years there was a lighting up of the active liver disease, again attended by perihepatitis, causing the intermittent pains, the fever, and the tenderness. The hernia operation instead of relieving conditions only exaggerated them, and the inflammation spread through the diaphragm, giving rise to a syphilitic pleuritis with cough and increased fever. It is even possible that a gumma in the liver became secondarily infected and that rupture through the diaphragm occurred. In any case, once the pleura was affected the effusion developed, due either to the inflammatory reaction of the serous sac or perhaps to blocking of some of the veins by thrombosis.

Such an enlarged and irregular liver of syphilitic origin is usually the seat of both gummata and diffuse gummatous infiltration, and eventually of scars which are left as the gummata are broken down and absorbed. The depression that was felt below the costal margin was doubtless due to a deep scar resulting from the regression of a large gumma. There may have been, in addition, some amyloid degeneration, but usually when such

change occurs it also develops in the kidneys and gives rise to albuminuria. This latter was not found in our case.

Splenic enlargement is quite commonly associated with hepatic syphilis, and this finding, with the large irregular liver in our patient, while, of course, not pathognomonic, should have raised seriously the question of syphilis in our minds. Gummata of the spleen are rare, and it is probable that the enlargement was due to a diffuse hyperplasia.

Pain and fever are present in many cases, the latter almost constantly. Usually the fever is moderate and of the intermittent type, but it is sometimes quite high and accompanied by chills, thus often with the local signs suggesting hepatic suppuration. The pain is supposed to be due to perihepatitis. Not infrequently when the pain is severe and occurs in definite attacks and the liver is not specially large gall-stones have been diagnosed. Portis<sup>1</sup> reports 2 such cases, both of which would have been operated upon but for the finding of positive Wassermann tests. Both cleared up under antisyphilitic treatment. Shrager<sup>2</sup> also reports a case in a woman of twenty-seven who for three years complained of severe paroxysms of upper abdominal pain associated with nausea, fever, and localized tenderness. The attacks came on every three or four weeks and often required opiates. At operation syphilis of the liver, and not gall-stones, was found. Wile,<sup>3</sup> too, has emphasized in recent years the sharp and paroxysmal nature of the pain that sometimes occurs. He quotes Klemperer to the effect that the fever is at times due to suppuration within the gummata.

In this connection Hunter<sup>4</sup> has reported 2 very interesting cases in which he believed there were actual gummatous abscesses. Both showed fever and rigors. One, a man of thirty-six years, had been jaundiced and vomiting for several weeks before admission to a hospital. He had several spells of fever, shivering, and sweating each day, the fever ranging from 97° to 105° F. This kept up for five weeks under Hunter's observation. Neither liver nor spleen was palpable at first, but later an irregular liver edge was felt. The leukocytes numbered 9000 to 11,000. There were signs of infection in the bases of the



lungs. Finally a positive Wassermann was obtained, and under appropriate treatment the fever subsided. The other case occurred also in a young person, a man of twenty-four years, who had had fever, upper abdominal pains, and vomiting for a week. He had had similar attacks two years before. On admission he was found to be jaundiced and seriously ill. There was abdominal distention and tenderness in the liver area, but the liver was not palpable. Moist râles were heard at his right pulmonary base and there were signs of fluid in that pleural cavity. Later a vague mass was made out in the gall-bladder area and the upper border of the liver was found to be at the level of the fourth rib. The fever ranged from 98° to 101.2° F. A subdiaphragmatic abscess was suspected and exploration considered, but the Wassermann test proved positive, and antisypilitic treatment caused immediate improvement. In this case, however, the fever did not entirely subside for four weeks.

Hunter felt that the diagnosis in the latter case was somewhat uncertain, but that syphilis was the important factor. He believed that a gumma had softened and formed an abscess, possibly due to secondary infection, and that the pleural and lung involvement might have resulted from rupture of this through the diaphragm or from extension through the lymphatics.

Our case in respect to the chest signs resembles this second one described by Hunter, but it seems to us unnecessary to assume an actual rupture of a gummatous liver abscess, since it is quite conceivable that the syphilitic process might spread directly through the diaphragm once a perihepatitis was well under way. The lymphatics might aid in this.

**Treatment and Results.**—While our patient was still under direct observation in the hospital, during her first admission, treatment was instituted. Because of the fact that the arsenic preparations are sometimes harmful in cases of liver disease it was thought wise to avoid arsphenamin for a time. She was therefore started on mercury by inunction, 2 to 5 grams of the official mercurial ointment being rubbed in daily for six days out of each week. At the same time iodids were given by mouth,

beginning with 5 drops of the saturated solution after each meal and increasing it steadily until finally, some time after her discharge, she was taking 50 to 60 drops after each meal.

On this régime she soon began to show steady general improvement, and when she returned to the hospital for follow-up observation about six weeks after discharge it was found that the liver had definitely decreased in size, the spleen was no longer palpable, her weight had increased to 140 pounds (from 123 on original admission), and in every way she felt better.

Next she was seen on June 17th, three months after her original admission, during which time she had faithfully kept up her mercury and iodid medication. It was then noted that there was only a slight difference in the elevation of the diaphragms and that they moved equally well. The liver was much less voluminous, though it still extended down to the umbilical level and in its lower part reached within 4 cm. of the midline of the body. The left lobe could no longer be felt and no irregularities whatever could be made out. The spleen was not felt. The general appearance of the patient was greatly improved. Her weight was 134 pounds. Blood was taken for a Wassermann, and this was still reported as strongly positive. It was advised that the mercury and iodids be continued and that in addition she be given a series of neo-arsphenamin injections.

On July 13th she received her first intravenous treatment (0.3 gm.) and subsequently had an injection (0.9 gm.) each week for six weeks. Now at the end of this time she returns for further observation and has again been admitted to the hospital for a few days in order that we might do certain liver functional tests and get another chest roentgenogram. You will note an appearance of good health. To inspection there is now no suggestion of trouble in the upper right abdomen, but by careful palpation the liver can still be made out as a thin mass in the right side. It projects downward almost to the umbilical level, but it is not at all voluminous and no irregularity can be detected. The spleen is not palpable. The right diaphragm is only slightly higher than the left and there are no signs of a pleural effusion.

A phenoltetrachlorophthalein test (Rosenthal), for estimation of her hepatic excretory function, was performed by Dr. E. Rose, our senior medical resident, yesterday, and he reports that fifteen minutes after 300 mg. of the dye were injected intravenously only 5 per cent. was left in the blood-stream, and that at the end of an hour none could be detected. This is, of course, a normal finding and indicates good excretory function. It shows that neither the liver disease nor the arsphenamin has caused any such functional disturbance. At the same time a Van den Bergh test was done to determine whether or not there might be any evidence of bile-pigments in the blood. The results from this test were also largely negative, there being no direct response (indicating no biliary obstruction) and a reading of only 1 unit by the indirect method which is slightly above normal and perhaps a little suggestive of hemolytic jaundice. Her Wassermann test is still strongly positive. A stereoscopic roentgenologic study of the chest shows no lung or pleural pathology, though the right diaphragm is even yet a little high.

We will now allow this patient to again return to her home and have her resume the mercurial inunctions and the iodid medication. After another month or six weeks we will advise another series of arsphenamin injections, and these alternated with the mercury and iodids should be continued until her Wassermann result is negative.

This case, therefore, is one of syphilis of the liver proved by Wassermann tests and the results of specific medication. The disease was probably acquired at about eight to ten years of age by contact with the dressings from rupial syphilids. The sudden onset of symptoms after an abdominal operation at eighteen years of age and the association of a right-sided pleurisy with effusion, probably syphilitic, are the unusual features of the case.

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## CLINIC OF DR. JOHN H. STOKES

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### CASE I. ILLUSTRATING THE SYSTEMIC SIGNIFICANCE AND DIAGNOSTIC INTERPRETATION OF PURPURA AND ERYTHEMA MULTIFORME

### CASE II. ILLUSTRATING THE DIAGNOSIS OF FACTITAL LESIONS

### CASE III. ILLUSTRATING THE CUTANEOUS ANXIETY NEUROSIS UNDER THE GUISE OF WINTER PRURITUS

### CASE IV. ILLUSTRATING THE DIFFERENTIAL DIAGNOSIS OF A LESION ON THE LIP

**Case I. The Systemic Significance and Diagnostic Interpretation of Purpura and Erythema Multiforme.**—You see before you a young colored woman, a teacher, twenty-seven years of age and married. Although chubby cheeked and even obese, she is obviously sick, and cannot obey your request to turn her head or expose her arm without pain, apparently referable to joints and muscles, especially about the upper extremities, shoulders, neck, and back. Her expression is slightly staring and anxious. Her voice is high pitched and querulous. There are no tics or spasms. Her respiration is rather rapid and superficial, but there is no evident dyspnea, no suggestion of air-hunger or stridor. Since we are to use her skin as a guide to her general condition, let us follow the custom of the dermatologist and examine before we ask questions or secure a history.

The skin of the body as a whole is that of a mulatto and is "warm, moist, and elastic," as the stock phrase used to put it. In spite of the racial pigmentation it is apparent that the girl

has a general eruption. While no one would propose it as an invariable rule, it is worth while to think of a general eruption of any type as suggestive of an internal rather than a purely external origin for the condition. Over the face there is an occasional deeper brown macule with a dusky bluish tinge. Over the trunk are numerous macules, diffusely scattered and of the same color as those on the face, but with a more distinct reddish tinge. The most significant and abundant part of the eruption appears upon the extremities. This fact, like the general distribution, suggests not only a systemic, but a vascular distribution, though here again caution must be used in constructing a general rule. The eruption as observed on the extremities consists of a series of lesions representing to some



**Fig. 144.**—Types of cutaneous lesions present in Case 1: 1, Purpuric macule. 2, Maculopapule with central softening and bulla formation (epidermis wrinkled and flaccid). 3, Annular flaccid bulla. 4, Annular papular lesion with central necrosis. 5, Purpuric maculopapule with central softening, ulceration, and necrosis. (The black center is slough.)

degree evolution stages of the original macular erythematous lesion. We find macules of the same dusky purplish color suggesting hemorrhage. We find maculopapules, we find papules whose centers are softening, and one or two even in which there is evident central necrosis. Some of the papules present denuded surfaces and superficial ulcerations which have been preceded by the formation of definite flat and flaccid blisters. We see deep papules or nodes, especially about the leg below the knee and about the shoulder—nodes which are obviously tender to pressure. On passing the fingers over the pretibial region tumid indurations, too diffuse to be visibly elevated, can be felt. In the white patient these would assume a pink color.

On the backs of the hands we see a small scattering of a very significant type of lesion—the ringed blister, or annular bulla. In some cases, however, we see rings, but the blister appears to be central rather than peripheral. The ring itself is papular. These lesions are few and confined to the backs of the hands.

On the mucous membranes we note a coated tongue with no lesions on dorsum or sides. Far back toward the fauces, but on the buccal mucosæ, there are superficial erosions covered with a pellicle more yellow than gray, a little thickened, a little crinkled and ragged and shreddy, for one composed merely of fibrinous and leukocytic exudate. The nasopharynx presents little of note. There is a leukorrheal discharge from the external genitalia, but no definite external lesion.

The palms and soles present an occasional pink spot, but no pronounced lesion.

From this description there stand out the following high points:

1. A general eruption, with blisters, and ringed blisters at that, among the lesions.
2. A localization of these lesions to the extremities, especially the backs of the hands.
3. Blisters combined with central necroses.
4. Tender nodes.
5. Lesions of the mucous membranes.

Macular lesions over the trunk, with some papules, and lesions on the mucous membranes, at once suggest syphilis to the majority of observers. Annular lesions tend to confirm the impression, for the annular papular syphilid is especially common in the colored race. But two items tend at once to remove this possibility from the differential field. The lesions are bullous, and blisters are practically unknown in adult syphilids, though common enough in infancy. Moreover, the annular lesions are on the extremities, where they seldom occur in syphilids, and the face, most often involved in the annular syphilid of the colored race, is free. These considerations serve to emphasize how vital to the diagnosis of a cutaneous

condition is correct observation of the distribution and the elementary lesion, and a stock of differential rules which enable one to apply his observations to the exclusion of one or another possibility. A diagnosis of syphilis had, in fact, been hazarded on this case, as it is repeatedly in cases of erythema multiforme.

In general I have found it more advantageous to consider the mechanism of formation of lesions of this type as a guide to their etiology, than to abruptly pass to the differential diagnosis. Lesions of general distribution, which are most abundant and severe upon the extremities, and in which the pathogenic agent is distributed to the skin by the blood-stream, form a large group of acute dermatoses, the erythema multiforme group, which ranges in morphologic appearance from macular eruptions of the most evanescent type, through purpuras, urticarias, nodose eruptions, combinations of urticaria, and bullous lesions, to necrotic centered papules such as are seen in the tuberculid. Variations upon the macular type are familiar in the exanthems of measles, and in the diffuse erythemas associated with scarlet fever. They occur with severe intoxications of unknown origin, as in scarlatiniform erythema, and with drug eruptions such as those of quinin and the salicylates. I think it may be roughly said that the more definite and ponderable and mechanical the cause of the vascular lesions, the more discrete the eruption and the more abundant and pronounced upon the extremities.

The essential lesion in the case of this young woman is produced by an infarction or injury of the terminal vascular cone in the skin. It is this fact that gives it its ringed character if superficial or its nodular character, if deep, and which is responsible for varying grades of injury ranging from mere slight redness and inflammatory reaction, to the gangrene of a complete occlusion of the blood-supply. The purpura in this case is a manifestation of vascular injury of a local rather than general character, for it is accompanied by a negative tourniquet test. The capillaries only give way at the point of application of the injurious agent from within, and are not diffusely injured as in the case of a circulating intoxicant such as bile in jaundice.

Reasoning backward from the dermatosis, then, this patient



has suffered a vascular insult of some description, which is probably due to the liberation into her blood-stream of mechanically distributed particles, *i. e.*, bacteria, that have injured or even totally occluded the vessels in which they have been deposited. In the skin the hemorrhages, exudation, and edema become visible to the diagnostician. They are, of course, no less real in the deeper tissues, and are undoubtedly responsible for the pain of movement which is so apparent. It is to be expected that vital structures will participate in this reaction to a bacterial "shower," and that the spleen, the liver, the brain and meninges will receive their share of the invaders.

It should not be too vigorously contended that the appearance of wheal-like and bullous rings with a purpuric macular eruption and inflammatory and tender nodes invariably means a bacterial shower, for it is well known that certain soluble agents, at least soluble on ingestion, such as iodids, or even bromids and salicylates, can give rise to these eruptions indicative of localized and apparently mechanical injury. On the other hand, it is more usual to find ground for suspecting a bacterial than a "toxic" agent in cases of this type.

A word as to the mucous membrane lesions. They are bullæ or blebs as a rule. In this respect they differ quite sharply from the eroded papules of the acute syphilids of the mouth. The shreddy or tough pellicle is really mucous membrane lifted from its papillary supports by fluid and then torn or ruptured. It is not the thin layer of pearly exudate over a dense lymphocytic infiltrate that covers the typical syphilitic mucous patch. For convenience I summarize this feature of the differentiation as shown on page 884.

By a process of reasoning from the cutaneous lesion and the mechanics of its production we have arrived at the significant diagnostic possibilities in the case. The young woman, regardless of the name by which we designate the cutaneous picture, is suffering from a vascular insult probably by a circulating mechanical and toxic agent of the type of a bacterial organism. The soluble possibilities, so to speak, should especially include iodid and bromid eruptions and salicylates.

*Mucous Lesions of Syphilis*

A ruptured bulla.  
 Pellicle tough, mucous membrane like, shreddy, yellowish.  
 Lesion actively inflammatory, mucosa livid.  
 Tongue comparatively often involved by papules on the dorsum.  
 Lips and mucosæ livid.  
 Intense fetor (in pronounced cases).  
 No bullous lesions, wheals, or iris lesions elsewhere.

*Mucous Lesions of Erythema Multiforme*

An eroded papule.  
 Pellicle thin, grayish or pearly, easily wiped off.  
 Lesion comparatively indolent, little vascular reaction.  
 Lesions rare on the dorsum of the tongue.  
 Lips and mucosæ normal color.  
 Little or no fetor.  
 Annular wheals with central bullæ most often on the hands.

The drug possibilities were eliminated by the failure to find any evidence either that she had taken or was eliminating any of the agents named. It should be noted that bromids may be retained and irregularly excreted, so that repeated tests of the urine should be made. Iodid and bromid eruptions are more apt to be pustular and vegetative, except in the fortunately rare acute and often fatal bullous form of iodism which is one of the gravest of drug idiosyncrasies. We are thrown back upon purpura and erythema multiforme as an expression of a bacteremia, as the tentative diagnosis.

In the light of the story of the case what shall we anticipate, and what shall be done to trace the cause and identify the nature of the bacterial agent?

1. *Physical Examination.*—Has the young woman a focus of bacterial infection which has "leaked" bacteria into her bloodstream? The two outstanding possibilities are streptococcal or tuberculous foci. There are no apparent foci in the mouth and throat, and no signs of a subacute but previously unrecognized bacterial endocarditis to explain a shower of streptococci into the blood. The question as to whether a biliary or other abdominal, or a pelvic focus may exist, needs full investigation, but at the outset certainly nothing supports it unless it be the leukorrhea, which is sometimes an accompaniment of arthritis, erythema nodosum and violent aphthous stomatitis and vulvitis in young women. The spleen is not definitely enlarged, but the obese abdomen makes decision difficult. The tuber-

culous possibility yields very little to physical examination, for there is no detectable glandular focus and pulmonary signs are lacking. Moreover, in my experience, pulmonary tuberculosis is not the type that gives rise to "tuberculous" purpura and erythema multiforme, which is in nearly two-thirds of the cases associated with glandular lesions. The glands, of course, may be retroperitoneal, associated as in 1 case I have seen with a tuberculous salpingitis, or they may be at the hilus of the lung. No tuberculous focus is apparent in this young woman, but her obesity, often seen in young women with tuberculids, and her age and race leave a lingering suspicion.

2. *Blood-culture.*—This appeals at once as the most direct approach to the question. But there is a flaw in the method, in that unless the young woman is actually continuously septicemic, a single culture or even repeated cultures may be negative. Moreover, the culture in relation to the bacterial shower is literally an afterthought in many cases, for the cutaneous lesions and symptoms which suggest the need for it follow the shower, and may not attract clinical attention until the organisms have disappeared. I recall, however, a case of "ulcerative purpura" in which purpuric lesions of wide extent with superficial necroses and ulcerations such as are seen in this case, were associated with a streptococcus and pneumococcus septicemia from which the patient recovered. In the septicemic stage of meningococcus infections cutaneous eruptions of this type may sometimes precede the development of meningeal symptoms. Moreover, if the bacteremia be tuberculous in origin, culture will be negative by the ordinary methods. In the case of this patient three cultures have been negative.

3. *Examination and Culture of a Lesion.*—If this is undertaken it must be upon the earliest lesion that shows definite infiltration. Bullous lesions become superficially infected almost at once. Serial sectioning may show bacterial emboli in the capillary loops as in erythema nodosum, and culture may identify them, though I would personally take a cultural result *cum grano salis*. Tubercle bacilli are rarely found in such

lesions, either because they are few in number or because they are quickly destroyed by the sharp inflammatory reaction.

4. *Examination of the Spinal Fluid.*—This is not a measure to be invoked at the outset. If the patient's meninges have escaped involvement in the "shower," it is still possible to provoke a meningitis by drawing off spinal fluid while the organisms are still in the blood-stream. On the other hand, if signs of meningitis appear, or there is no recrudescence of lesions after the first crop, a puncture is indicated, drawing as little fluid as possible. If the exudate is polymorphonuclear, it is often advised that antimeningococcus serum be introduced at this time.

This series of considerations carries us, of course, directly into the internal medicine of the skin lesion. We find that this patient had had a previous admission to the University Hospital four months ago for pleurisy, from which she had recovered without residua, in two weeks. There had been no cough or expectoration of blood suggesting embolus at that time. The onset of the present illness had been violent, with a chill, high fever, delirium, vomiting, and headache. The patient had been semicomatose on admission, blood-pressure 70/52, pupils fixed, no true stiff neck. The temperature had steadily risen, leukocyte count 27,500, hemoglobin 85 per cent., platelets 40,000. In the course of four weeks the hemoglobin has fallen to 65 per cent. The fundus examination showed no hemorrhages, and no tubercles in the choroid, where they are sometimes early recognizable. The blood Wassermann reaction was negative, urine negative. Only Vincent organisms and diphtheroids, the ordinary culturable saprophytes of the mouth, were found in the lesions on the mucous membranes. The cutaneous lesions began to involute in about a week and no new crops developed. Joint pain subsided, but the neck became gradually stiffer, Kernig sign negative, however. When the stiffness of the neck became definite, lumbar puncture was done, and a cell count of 1800 cells per cubic millimeter, 85 per cent. polymorphonuclears was found. The Wassermann on the fluid was negative, the colloidal tests negative, the fluid pressure not much increased, the culture negative, and there were no organisms in the smear.

Guinea-pig inoculations have been made but, of course, cannot yet be reported. Antimeningococcus serum was administered intraspinally. The patient is showing a slow improvement, the temperature is subsiding, no endocarditis has developed, but there have been mental symptoms at times.

Thus far, then, the diagnosis is not determined. As a dermatologist I may say, however, that I have seen purpura, erythema multiforme, and erythema nodosum precede, with almost complete recoveries for periods of weeks or even months, a final decline from miliary tuberculosis or an acute death from tuberculous meningitis. Not a few details in the present case, including especially the previous pleurisy, the relative mildness of mouth lesions and the chronicity of the affair with negative bacterial findings in the presence of such a pleocytosis in the spinal fluid, lead me to suspect that we may have witnessed a cutaneous and systemic reaction to a tubercle bacilleemia.

**Case II. Diagnosis of Factitial Lesions.**—There is a piece missing from this woman's nose (Fig. 145). This must be apparent even from the back seats—and it is, in fact, the first diagnostic consideration. The decision that one is dealing with a *destructive* lesion of the skin sets in motion a train of serious considerations. In effect, by this item alone, we are called upon to weigh the possibilities of:

- The granulomas.
- The malignancies.
- Adventitious trauma.
- Self-inflicted trauma.



Fig. 145.—Diagrammatic profile of the face, showing the factitial lesion of the ala of the nose in Case II.

## Gangrene:

Toxic.

Vascular.

Bacterial.

Chemical.

Mechanical.

It would contribute materially to acuteness in general diagnosis if we would adopt for our cutaneous outlook on medicine the slogan "Never let a destructive lesion of the skin go unexplained."

We see, then, a destructive lesion which has removed with the precision of a punch a demilunette of tissue, skin, cartilage, and mucous membrane 2 cm. in diameter, from the left ala of the nose of a woman in middle life; a woman quiet, perhaps bovine in demeanor, submissive, credulous, and yet a bit canny at that, as you shall presently see.

The margins of the lesions seem perfectly healed. There is a slight irregularity with a little paling of the edge such as one sees in the skin over healed cartilage, which is not to be confused with the pearliness of epithelioma. There is a little redness about the periphery, but on glass pressure there are no demonstrable minute apple-jelly colored puncta which mark the presence of the cutaneous tubercle. The mucosa of the nose is slightly crusted and there is healed scarring where the tissues have been exposed, and perhaps involved in the injury. But there is no evidence of a pearly border or translucent tubercles, no papillomatous border of blastomycosis.

Perhaps this was at one time an ulcer, but such perfect definition of the tissue loss suggests rather a slough. What might produce a circular slough in such a situation? The granuloma most prone to produce sloughs is, of course, syphilis through its action on the blood-vessels. Yet there is little or nothing to suggest syphilis about this woman, and syphilis is rarely monosymptomatic. Mother of 6 healthy children, with every possible excuse for miscarriages, but having had only one, and that recently, and with a gangrene well to one side of tip of the nose instead of on the end or on an extremity where it would be most

likely to appear, is against syphilis as the cause. The lesion is too complete, too final, too scarless for the usual syphilids, the surrounding tissue too entirely uninvolved, the cartilage, less often attacked in syphilis about the nose, too evidently involved here to the same extent as the skin. If the lesion is not likely to be tuberculous because so obviously healed, or syphilis for the reasons mentioned, we fall back on malignancy. Does epithelioma on the skin heal itself? Sometimes, though rarely completely. An epithelioma that attacks the cartilage is least likely to do so. Yet there remain no evidences on the surface of epithelioma.

It is vital at this point to impress the need for a painstaking internal examination of the nose, for treatment may have disposed of the external disease, leaving a small malignant ulcer within. The special nose and throat examination discloses nothing. Does that settle the question? It certainly does not. Regardless of what diagnosis we shall reach, we know at the outset that we shall require time and observation here if the patient is to be fully protected against error.

Of the traumatic factors, adventitious sources are objectively removable because there is practically no form of accidental injury that could thus punch out the ala. Of deliberately inflicting injuries we confront at once, of course, possibilities that can be eliminated to some extent by the history. There are, however, two types of injury of which it will be difficult to obtain a history—injury of which the patient is ashamed and injury which is self-inflicted. The chemical injuries include among the gangrene or necrosis-producing agents, first, strong alkali, always available in the form of potash lye; second, pure phenol; third, concentrated acids, including nitric acid, with its yellow stain, and sulphuric acid, with its black slough and surrounding inflammatory reaction; and finally, arsenic, represented by the arsenious acid paste. Bacterial gangrenes, including noma and Vincent infection, are obviously hardly applicable here.

It would appear to be the simplest thing in the world to ask this woman what she has been using. But she gives even to

repeated questioning no history of using anything. The trouble began more than three years ago as a pimple on the side of the nose. The physician to whom she went, and who cut it off and touched it with caustic, has since died. The wart returned, grew, finally became black, and dropped off, leaving the present defect. In vain do we attempt to persuade her that she or some one else has made applications. She stoutly denies it. (At this point the patient is taken from the room.)

Yet a week later, when she found her stay in the hospital getting wearisome, when the doctor told her everything was negative, and when I kept gently reiterating and reminding her that there must be something back of it all, she herself came to see the need for our knowing all there was to know about it. In the quiet of the evening, when we were just visiting the ward, as a friend and not, please note, as the triumph of a third degree inquisitorial presentation or before a clinic, we "got the story" as the reporters say. She showed me the hard black slough she was keeping as a souvenir, and as I pondered over it, she said she didn't tell us something at first because "she thought we regular doctors didn't believe in charms." She had been to a "charm doctor" in a nearby town when the wart came back. He had put "a piece of cheese-cloth on it" and there it had stayed for five weeks, at the end of which time the charm worked and the black piece fell out. The "doctor" had told her "it would be like God himself come down and cut the roots out of it like a knife." The cancer plaster did its work. When a patient uses the word "roots," dig for the cancer quack in the history.

Observation, then, until the possibility of malignancy is laid to rest (for the original lesion may have been malignant) and then a plastic restoration summarizes the management of this case. The diagnosis was reached by a friendly gaining of the confidence. In some patients with self-inflicted lesions it may be necessary to use dragooning methods, where the malingering is a well-planned scheme. But with the hysteric or half-frightened victim of a factitial lesion the best diagnostic and reconstructive result is won by kindly insistence.



Remember that the keynote of a factitial lesion can only be found in the fact that it "won't fit in." It is bizarre. Sometimes it is recognizable as a case of "they ain't no sich animal" on sight. Sometimes the facies of the patient, that curious and indescribable mixture of obstinacy, bravado, guilt, and the "bed-room eye," betrays him or her. But, again, the diagnosis may be made only by a contribution of inexorable logic which says it doesn't belong among the reasoned possibilities, and that leaven of human insight which should be the heritage of the physician.

**Case III. Cutaneous Anxiety Neurosis Under the Guise of Winter Pruritus.**—Mrs. B. says that her skin scales and itches, and that her husband and son have the same "disease." In fact, she feels they caught it from her.

In examining Mrs. B. privately the scaling was easy to find. There was a slight furfuraceous exfoliation over the pretibial region. The skin over the knees was a bit thickened and hyperkeratotic. The forehead was a bit dry and scaly. There was a definite seborrheic eczema of the scalp, but, take it all together, with no inflammatory changes, there was too little to be found for the insistence and magnitude of the patient's complaint. Examination of the palms, so often the crux of diagnosis in a patient who complains of scaling, itching, and dryness of the skin, showed a definite suggestion of the parchment wrinkling and dryness characteristic of ichthyosis. It is curious how often a mild degree of ichthyosis, overlooked, contains the kernel of cutaneous diagnosis. It is often the basis of the form of itching which makes many persons uncomfortable after the dry heat is turned on in houses in the fall of the year. The skin, none too liberally supplied with fat from birth in these individuals, becomes more dry and scratchy than ever under the combined irritations of a dry atmosphere and heavier underwear, especially if it contains wool. While winter pruritus, so-called, may occur in patients who are not ichthyotic, the congenitally dry and scaling skin is often the basis of the trouble. In such cases the scaling is most marked over the sites noted in Mrs. B., and

there is apt to be also an accentuation of the hair follicles, often with actual plugging over the extensor surfaces of the upper arms. The seamy, dry, parchment palm is, of course, the most distinctive feature. I have even seen the scaling and slight irritation of the skin in an ichthyotic child interpreted as the exfoliation of scarlet fever without rash, following a severe streptococcus throat.

Mrs. B. notes relief when she applies a grease to the skin, and this is, in fact, the only treatment indicated for the actual cutaneous condition. Olive oil and lime-water emulsion, liberally applied after the weekly bath with a few drops of oil of bitter almonds for "flavor," is an excellent preparation. Old-fashioned goose grease and the refined lanolin known before the war as eucerin are very satisfactory. Patients must be warned to use less soap. Most of them are possessed by the demon of cleanliness. But of all these practical instructions little heed is taken by Mrs. B. She returns insistently to the fact that she sees the scales floating in large amounts upon the bath water, and to the obvious contagiousness of her condition as evidenced by the fact that her husband and son are scaly in her sight. She is evidently very much upset over it, wringing her hands silently, her chin twitching, eyes on the verge of tears.

The earmarks of the dermal anxiety neurosis, if we may call it such, nearly always include several of the following elements: itching with no obvious cause; a periodicity in time that suggests psychic influence, such as a definite hour of beginning or ending; the idea that a parasite is present, which the patient will eagerly demonstrate; the belief that the condition is contagious; and some element of self-blame, as of the transmission to a loved person, etc. The obvious cases, such as acarophobia, the belief that one is infected with parasites when none can be found, are easy enough of recognition. The atypical cases, however, wander from doctor to doctor before getting set right, granted that setting right is possible by anything short of a complete psychoanalytic reconstruction. Among the commonest forms of dermal anxiety neuroses with which I am acquainted are:

The belief that hair is falling out.

The belief that excess hair is growing.

Delusions of cutaneous parasitism.

Diffuse itchings and scalings.

Pruritus vulvæ.

Hair pulling (trichotelomania).

Acne excoriee des jeunes filles.

The typical example of the first condition is found in the school-teacher who is trying to make ends meet in support of an aged mother on the beggarly salary of an educator. The fear that she must give up work because of some personal disfigurement is often the first warning of that period of nervous breakdown which temporarily invalids the high-strung, overloaded unmarried girl in her early thirties. Imaginary hypertrichosis follows severe nervous shocks, as, indeed, do any of the dermal neuroses. Acarophobia may, of course, reach the proportions of a genuine insane delusion. The patients insistently exhibit bits of traumatized flesh, small crusts from excoriated papules, and many even point to small senile angiomas, normal in the skin after forty, as parasites. Of the itching and scaling type Mrs. B. is an example. Pruritus vulvæ seems most apt, though not invariably, to develop in the neuropathic girl who has had an unfortunate affair of the heart, especially if it has been accompanied by clandestine sexual activities. The association is not so absurd or impossible as it seems, and the most extraordinary facts sometimes are elicited in confirmation of a suspicion. Unconscious pulling of hair and eyebrows is not so very rare. The "acne excoriee des jeunes filles," whose French name explains itself as the acneiform excoriation of the face (or for that matter of the body) produced by the sedulous "squeezing" of real or imaginary pimples by nervous young women of the office or boarding school type, often has its basis in some repression and frustration or some irreconcilable conflict in the deeper personal life of the individual.

Mrs. B. and I went over the situation in some detail after I had "rushed her defenses," so to speak, by saying suddenly that she must have been through some crushing experience lately. This rather generic remark, applicable in one way or

another to most of us, acts like a fly cast at a trout in the patient who has a dermal neurosis, and is apt to be greeted by a burst of tears and the gradual capture of the conflicting complex if the patient is not too difficult. Fishing of this sort is no affair for the tyro, for it sometimes leaves the patient worse unstrung than before, and may fail so completely that only an established reputation and self-confidence can stand the blow. But in more than half the cases I have met, the quiet explanation after a full hearing, of the mechanism of the anxiety neurosis has done much for the patient. It should be explained as the effort of the mind to build up a defense of tangibilities and realities against the oppressions of the intangible and unbearable, to substitute a supposed bodily ailment or pain for an incomprehensible and uncontrollable mental anguish. This enables the patient first of all to rationalize the delusion, and then slowly to re-educate herself to its unreality and to escape from it. After half an hour's talk, in which I heard Mrs. B.'s story of the loss of her mother, assured her that the flakes in the bathtub were calcium oleate or hard soap, that her son at least had acne and seborrheic dermatitis and not infectious scaling, and that the relief she got from greasy applications was real relief, the nearest thing to cure that could be had, the patient left the clinic apparently on the road to reconstruction. Usually the first interview determines the result, and it should be as long, as frank, and as dispassionate and kindly as the occasion demands. Patients who come back or who start another medical round must usually have the services of a neuropsychiatrist for recovery, if they recover at all.

**Case IV. Differential Diagnosis of a Lesion on the Lip.—**

Mary N., apart from her puffed upper lip (Fig. 146), is a healthy, rather fat, young married woman of twenty-three years. She has had one miscarriage and given birth to one healthy child. Her husband, a drunkard, has deserted her. About a year ago she developed what appeared to be an infected cold sore on the upper lip, which came and went, sometimes larger, sometimes smaller, under the influence of ointments and local applica-

tions. Of late she has received drops of some sort, which partly cleared up the lesion, but on stopping the medicine the rate of growth seems to have been redoubled, and the progress of the involvement of the upper lip can be seen easily from day to day. The lesion is a brownish red fleshy tumor with a flange-like extending periphery and a slightly depressed center. There is no ulceration, no pain or tenderness, no scar. One fact of diagnostic importance is the presence of a satellite lesion to the left of the larger growth on the other side of the lip and completely separated from it.

On the upper lip the possibility of malignancy seems to be among the first to occur to the practitioner when a papule



Fig. 146.—Gumma of the upper lip (Case IV).

begins to mushroom out in this fashion. Yet in my experience malignant lesions of the upper lip are distinctly less common than those of the lower lip, while the other possibilities—tuberculosis, gumma, chancre, pseudochancres, sарсoid, vegetative dermatitis, and blastomycosis—come to the front.

The flange-like periphery, of course, suggests epithelioma, but the acuteness of the recent growth, the inflammatory character of the lesion, the absence of the hard pearly nodule with its little rim of dilated capillaries visible under the lens, is all against it. Moreover, the satellite, and the come and go of the lesion, are flatly against epithelioma. An essential move in the diagnostic technic is the examination of the lesion under glass pressure, which may be exerted with a thick tumbler edge if

no diascope is at hand. Such a maneuver may disclose small tubercles (apple jelly nodules) in the blanched surface at the periphery. Glass slides have a trick of breaking at the critical pressure. The giant chancre of the lip is firmer, eroded, or ulcerated, of shorter duration than this lesion. Yet it is never amiss to secure some serum for dark-field examination. The pseudo-chancro redux or gummatous recurrence and the true gumma will give negative dark fields, the chancre will give a positive in the first few weeks of its course.

Sarcoids, rarely seen about the lip, but often about the nose and cheek, are tumors or plaques of tuberculoid histologic architecture, of a fleshy tint and consistence, sometimes raised, bluish or brownish red, sometimes merely nodular or diffuse subcutaneous infiltrations, which respond to some extent to arsphenamin, and hence may be mistaken for syphilids. Vegetative dermatitis usually presents the mammillated surface and pus crypts of the pyogenic granuloma, but may at times, on the lip, form the sessile or pedicled dark red, easily bleeding tumor formerly thought to be a mycotic infection or a sarcoma, but now known to be merely a highly vascular granuloma of pyogenic origin. In ulcerative lesions of the upper lip, unlikely though it may seem, chancroid must not be overlooked.

The adenopathy for which one always feels in these cases is usually late, small, and hard in malignancy; early, large, unilateral discrete and not tender in chancre, and late, apt to soften and break down in an inoculation tuberculosis or sporotrichosis.

Blastomycosis is also unusual on the upper lip. This infection, like sporotrichosis, seems to be relatively rare in the eastern United States and more common in the Middle West. The earmark of blastomycosis is the extending papillomatous border with central contractile scar, and the minute epithelial abscess, found between the papillomatous projections of the margin. On pressure with a ring curet over the margin several minute droplets of pus can usually be made to exude. In this pus the blastomycete may be found, a typical yeast with double refractile wall and budding forms. The diagnosis should not be attempted by the inexperienced on microscopic grounds alone.

The border and surface of this lesion is smooth, there is no papilloma, and there are no abscesses, so that blastomycosis is readily eliminated.

Sporotrichosis of the upper lip, while rarely resulting in such a tumor as this before metastasis to the adjacent lymph-nodes and skin has taken place, must never be lost sight of. Cultures should always be taken on lesions of the lip if they are softened or ulcerative. Maltose agar and room temperature is needed for sporothrix.

The differential diagnosis in this case proved especially difficult because of an item in the history relating to a brother who lives with the patient. He has a cough with much expectoration and is rapidly losing weight. It was impossible to reach him for examination, but such a history may cover the background on which an inoculation tuberculosis of the lip, superimposed on a herpes, may develop. While the patient was herself not a victim of pulmonary tuberculosis from which orificial tuberculosis might have originated, we felt it necessary to eliminate the tuberculous possibility by removal of tissue. A warning is necessary as to the interpretation of such findings, for especially about the mucous membranes, in my experience, has it been easy to confuse the histology of gumma and tuberculosis, unless one insists upon the demonstration of absolutely typical and unescapable tubercles, and not merely giant-cells and inflammatory changes. Animal inoculation from the excised tissue is always desirable. In this case a wedge of tissue removed from the flanged edge showed merely chronic inflammatory changes. To the physician who hesitates to take a biopsy in such a site for fear of disfigurement, it may be said that a wedge cut with a cataract knife under local anesthesia and not closed by stitches, will leave almost no scar distinguishable from the remnants of the process itself after involution. It is not necessary to invade the margin of normal skin.

But why wait so long to mention the Wassermann test? Because we should train ourselves to independent clinical judgment in all our dealings with the skin and use the Wassermann reaction as confirmatory rather than crucial if we can. Mary N.'s

blood Wassermann reaction was strongly positive. The involution of the lesion under treatment for syphilis was immediate, the deformity practically nil. It is really amazing how complete and satisfactory may be the involution of gummas of the lip. The residual pigmentation will ultimately disappear and there will be only the slightest atrophic non-contractile scarring. Our obligation toward her syphilitic infection is not ended, however with the involution of the lesion, for she has a living child, a presumably infected husband who cannot be found, and may herself have visceral and other lesions of the disease which call for spinal fluid examination and for prolonged observation and treatment.



## CLINIC OF DR. JAMES E. TALLEY

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### PUERPERAL HEMIPLEGIA

TURNING from the study of the heart in pregnancy, there is a rare, closely related subject which merits our attention. Puerperal hemiplegia interests the cardiovascular student as well as the obstetrician and neurologist.

My interest was aroused in this subject by a patient seen with a colleague some months ago. The patient, aged thirty-two, primipara, was delivered at term by version by a skilful obstetrician. There was a supposition that all was not exactly right when she entered the hospital, as she had complained of a slight cold and her temperature was a few fifths above normal. After delivery a temperature of 99° F. with slight acceleration of the pulse persisted. Suddenly on the seventeenth day she became comatose and a *left-sided* hemiplegia developed at once, though its degree increased for a time. The left face, arm, and leg were involved; the stupor was too great to be sure about speech. This was partly due to an opiate given to alleviate the distress of a painful clonic movement of the left hand early in the attack. There was Cheyne-Stokes breathing the first four nights. A week later she was conscious, the speech connected. The whole left side was paretic, left arm especially flaccid. The left hand could be moved slightly at the wrist. The left leg could be lifted from the bed. Left knee-jerk, ++. Right knee-jerk, free. Pulse 88 to 114. Temperature 99.2° to 99.6° F., once mounted to 101° F. A few days after the palsy the right leg became painful. It was now 1 cm. larger than the left. The thighs were equal. The heart appeared normal. Four months later the left arm is paretic. Otherwise

she is normal. The slow development of the palsy speaks for thrombophlebitis. The femoral phlebitis points to the focus of infection. Here, however, the primary involvement was in all likelihood in the uterine veins with gradual extension to the femoral. This is a common history in such patients. Phlebitis of the uterine veins is a latent process, rarely recognizable during life.

Puerperal hemiplegia has been attributed to thrombophlebitis, embolism, cerebral congestion and edema, cerebral hemorrhage, brain abscess, and even severe anemia. It is a rare condition, and yet enough cases are recorded with autopsies to make one feel that thrombophlebitis and embolism are the underlying causes more often than cerebral hemorrhage.

**History.**—Hippocrates spoke of newly delivered women with some part of their body rendered powerless.

In 1828 Ménière<sup>1</sup> published 5 cases of hemiplegia occurring during pregnancy or parturition in whom the autopsies showed cerebral hemorrhage. This was the first scientific explanation offered.

In 1869 DeCorniere<sup>2</sup> added puerperal endocarditis to the already known causes of puerperal hemiplegia.

In 1872 Charpentier<sup>3</sup> made a serious study of the pathology of the condition. Darci,<sup>4</sup> 1877, and Raymond,<sup>5</sup> 1880, reviewed the subject. Most of these contributions were theses for the doctorate in medicine, as was that excellent contribution of A. Lafon,<sup>6</sup> who collected 25 cases in 1896.

Beginning at the present and working backward for some years we have found 9 cases; adding these and our own to Lafon's 25, we have 36 cases for study.

**Outstanding Clinical Features of Puerperal Hemiplegia.**—It is usually a hemiplegia. Both extremities need not be equally affected, though the arm is apt to suffer most. Monoplegias occur. A primary partial aphasia is sometimes the forerunner. In the 36 cases, there was *right*-sided hemiplegia in 17, *left* in

<sup>1</sup> A. Lafon, Contrib. a l'etude d. l'Hemiplegie Puerperale, These de Paris, 1896.

<sup>2</sup> Ibid.

<sup>3</sup> Ibid.

<sup>4</sup> Ibid.

<sup>5</sup> Ibid.

<sup>6</sup> Ibid.

10; in 9 the side was not recorded. The greater frequency of right-sided hemiplegia has an anatomic explanation as far as embolism is concerned. The left internal carotid arises straight from the aorta, offering a free course to emboli. The right brachiocephalic comes off obliquely. In this series there were 17 deaths, 18 recoveries, and result not known in 1.

The autopsy reports seem to point to the causes of death in this series in this order: cerebral thrombophlebitis 7, cerebral hemorrhage 3, thickened meninges 1, cerebral embolism 1, brain abscess 1, no necropsies 4.

That this is a fair ratio for embolism seems unlikely, as embolism must frequently be the precursor of the cerebral thrombophlebitis secondary to masked or even frank pelvic phlebitis.

The days of onset were: first week, six; second week, fourteen; third week, eight; fourth week or later, six.

Nine were primipara, 2 followed the second birth, 1 each followed the fourth, fifth, sixth, seventh, and eighth births.

Just how many had a primary phlebitis in pelvis or leg, frank or concealed, is uncertain. Many had, and in several the hemiplegia preceded the detectable phlebitis.

**Pathology of Puerperal Hemiplegia.**—*Thrombophlebitis.*—In puerperal infections, however mild, all the elements necessary to thrombus formation are present—bacteria to injure the intima, sluggish circulation to favor the deposition of blood-platelets on the necrotic wall, which sets in motion the chemical changes leading to clotting. In arteries the chief causes are disease of the vessel wall and embolism; in veins infection which leads to injury of the intima. In puerperal infection streptococci, staphylococci, and other pyogenic bacteria are chiefly concerned, and they all show a great predilection for the veins.

Puerperal thrombophlebitis may be found in uterine, pelvic, iliac, femoral, saphenous, or any veins in these regions. It may be confined to a small area or be wide-spread. In comparing the seats of thrombosis in puerperal, postoperative, and general medical statistics one is struck by the uniformity of location, generally speaking, in all three conditions. This ob-

servation appears to support Aschoff's opinion that disturbed blood flow is an important factor in thrombus formation. This idea in nowise detracts from the importance of the infectious factor. Often this thrombophlebitis remains localized in the lower part of the body, but too often it spreads by means of blood-stream and perhaps lymphatics elsewhere. From these foci cerebral embolism and thrombophlebitis of cerebral veins and sinuses arise, causing puerperal palsies. The possibility of an embolus passing through the pulmonary capillaries will be discussed under Embolism.

The degree of latency in pelvic thrombophlebitis is remarkable. Frequently in the cases the writer studied, first came the sudden hemiplegia in a woman doing well and later the phlegmasia declared itself.

Williams<sup>1</sup> once found at autopsy the femoral vein and all its branches occluded, yet careful measurements were necessary during life to detect any difference at all in the size of the leg.

The evidence of phlegmasia was trivial in the case of puerperal hemiplegia seen by the writer, and it appeared three days after the palsy.

It is not an uncommon experience for pulmonary embolism in the puerperium to herald the presence of an unexpected pelvic phlebitis. Such latent attacks are more prone to arise in the pelvic or uterine thrombophlebitis than in phlegmasia.

The phlegmasia may be hidden or appear unimportant, but the embolism may prove fatal, as Remy<sup>2</sup> found in 3 patients. In these hidden cases at autopsy but a slight phlebitis in uterine or broad ligament veins may be found; even this may be lacking. The autopsy may read "uterus small, firm, clean, appearance normal," as in Hunt's well studied case, and yet the infection had produced wide-spread fatal cerebral thrombophlebitis and sinophlebitis. Statistics on puerperal cerebral thrombosis, puerperal cerebral embolism, and puerperal hemiplegia are meager. In general puerperal thrombophlebitis and pulmonary embolism

<sup>1</sup> Williams, Text-book of Obstetrics.

<sup>2</sup> Remy, *Rev. France de Gynec. et d'Obstet.*, 15, 172, April, 1920. *Abs. Jour. Amer. Med. Assoc.*, 75, 278, July 24, 1920.

they are more satisfactory. Puerperal pulmonary embolism is much commoner than puerperal cerebral embolism. It is by comparison of these statistics that we get a relative idea of the frequency of the real subject under discussion.

Klein<sup>1</sup> collected 113,459 cases of labor in various clinics. The average percentage of thrombosis in all the clinics was 0.81 per cent.; it ranged in individual reports from 0.12 to 2.5 per cent. Pulmonary embolism varied from 0.04 to 0.3 per cent. To Klein an aseptic thrombophlebitis in the puerperium does not exist.

Junge<sup>2</sup> found in 10,050 births 81 cases of puerperal thrombosis, 0.8 per cent. There were but four embolisms (pulmonary apparently) in the 81, 0.04 per cent. He found varices in 26.8 per cent. of the women in the Strassburg Clinic. Throughout the literature, however, there seems to be a general agreement that puerperal embolism much more frequently arises in uterine or pelvic thrombophlebitis than in the thrombophlebitis of a superficial vein.

That many of his cases had old heart disease and many had lost a large amount of blood from parturition are important observations.

Ritzman<sup>3</sup> found 55 cases of pulmonary embolism in 6000 necropsies, and on only 6 rapidly fatal cases was an exact diagnosis made during life. One is sure his clinic is not unique in this respect. We will recur to this subject under Embolism.

Rupp<sup>4</sup> found embolism or infarct of the lungs in 5 per cent. of the 12,971 necropsies done in eighteen years. In 22,689 operative cases in eighteen years, 0.26 per cent. died of thromboembolisms. In 5300 dying of internal diseases in the same period, 1.1 per cent. had thrombophlebitis. As remarked before, the great similarity of the primary seats of the thrombophlebitis in all three series is noteworthy.

None of the statistics refer directly to puerperal hemi-

<sup>1</sup> Klein, *Arch. für Gynæk.*, vol. 94, 1911, S. 251.

<sup>2</sup> Junge, *Arch. für Gynæk.*, vol. 96, 356, 1911.

<sup>3</sup> Ritzman, *Berl. Klin. Wochenschr.*, 1911, vol. 48, p. 1330.

<sup>4</sup> Rupp, *Arch. für Klin. Chir.*, 115, 689, March, 1921.

plegia, but Harrar,<sup>1</sup> in investigating the causes of maternal death in 100,000 cases of childbirth, finds three leading groups in order of morbidity. The largest group begins with puerperal infection and eclampsia, the less severe group begins with nephritis and cardiac decomposition, and in a third minor group he finds 1 to 3 deaths each due to pulmonary embolism and thrombosis, cerebral hemorrhage, and abdominal pregnancy.

*Cerebral Embolism.*—If pulmonary embolism occurs in but 0.04 to 0.3 per cent. cases with thrombophlebitis, then cerebral embolism is less and puerperal hemiplegia still less. All these are comparatively rare yet, like a ruptured ectopic pregnancy, they make a dramatic entrance and their victim a no less dramatic exit only too often. Furthermore, though rare, they sometimes run in schools as it were.

Hans Michaelis<sup>2</sup> in the first weeks of his private practice lost a patient with pulmonary embolism. In the next six months he had 2 private patients with femoral thrombosis and pulmonary embolism, both fortunately recovered. In two years he had 8 cases of pulmonary embolism with apparently but 2 deaths. The 2 deaths, one in ten minutes, the other a half-hour, are enough to whet one's diagnostic acumen.

Davis<sup>3</sup> quotes Sears as having found 107 cases of pulmonary embolism in 3006 necropsies, a large percentage not diagnosed. There is an excuse for missing at least some of the pulmonary emboli found postmortem. Karsner and Ghoreyeb<sup>4</sup> found experimentally that a simple embolus interfering with less than an entire lobe of the lung gave origin to little circulatory disturbance owing to the rich anastomosis of the pulmonary artery between its own branches. Large emboli block the pulmonary artery and kill, not so much from their influence on the lung as from the sudden strain thrown upon the heart. Lesser emboli give a picture of pleurisy or pneumonia, some perhaps of pulmonary edema, and some remain quiescent as they frequently

<sup>1</sup> Harrar, Bull. Lying-in Hospital, New York, 1916-18, p. 257.

<sup>2</sup> Hans Michaelis, Centralblat. für Gynæk., 1911, No. 30; Zeitsch. für Geburts. und Gyn., vol. 70, 1912, S. 278.

<sup>3</sup> Davis, Med. and Surg., 1917, April, vol. 1, 198.

<sup>4</sup> Karsner and Ghoreyeb, Jour. Exp. Med., 18, 507, 1913.

do in spleen or kidney. Such cases are found among those studied, and frequently the area giving symptoms of embolus is not the only one thus affected. In some cases studied there have been in the same case pulmonary embolism, hemiplegia (cerebral embolism), and embolism of superficial veins. These multiple emboli arise in a recurrent endocarditis.

MacCallum<sup>1</sup> says infarction of the brain is extremely common; if it occurs in the meninges it may be symptomless. If a small vessel alone is involved, there may be a temporary lapse from consciousness or none at all. There may or may not be variously localized palsies. If the branch is large, symptoms like apoplexy occur, unconsciousness, a flaccid palsy more widespread at first, and a limited palsy will persist corresponding to the part of the brain destroyed.

In autopsies of cardiacs of long standing the pigmented scars of old infarction may be found, all near the surface of the brain without any history of symptoms.

If the emboli are septic the first effect is mechanical, then the infected area becomes the seat of acute inflammation, softening, and disintegration from the ferment of the bacteria and the rescuing leukocytes. These areas in the end resemble an abscess.

Herein one finds one explanation for the transitory aphasias and hemiplegias found in some of our histories.

Puerperal embolism should lead us to seek for an endocarditis recurrent during pregnancy or arising from puerperal infection. A latent and unsuspected acute endocarditis is sometimes found at autopsy in these cases of puerperal hemiplegia.

Now as endocarditis more often involves the left side of the heart, there is no question that emboli may be swept thence to the brain. But how is an infection carried from uterine, pelvic, or femoral veins to the brain, as it evidently was in some of the cases collected, or how else explain the sudden hemiplegia? *Can an embolism, however small, pass through the pulmonary capillary network?* We think MacCallum answers the question as to the mechanism. The passage of thrombotic

<sup>1</sup> MacCallum, Text-book of Pathology.

fragments may be problematic, but he includes "clumps of bacteria" among the various kinds of emboli. He adds: "Bacteria may enter the blood-stream by growing through the walls of the capillaries or by being discharged from infected thrombi, and, as is well known, *circulate with the corpuscles of the blood through any capillaries.*" Once having passed through pulmonary network the bacteria can set up the same pathologic process on the systemic side of the circulation, whether it be in heart valves or cerebral vessel itself. It is conceivable that even a clump of bacteria themselves might plug a small terminal artery.

Again, they can set up a new thrombophlebitis in the systemic circulation and give origin even to new emboli. This may explain some of the sudden hemiplegias with well recognized primary focus in the femoral.

Some writers speak of a paradoxical embolism, the embolus from the right heart passing through a patent foramen ovale. This would explain but a limited number of cases and is put forward on theoretic grounds. No such case was found post-mortem. Siemerling<sup>1</sup> recognizes the difficulty, but admits the possibility of a very small emboli passing through the pulmonary capillary.

Daels,<sup>2</sup> from his experiments with intra-arterial injections of virulent tubercle bacilli, has no doubt of it.

Rossier<sup>3</sup> in the same discussion says, as all agree, the commonest metastasis from pelvic thrombophlebitis is in the lungs, and he implies there may be a primary pulmonary localization whence arises new metastasis to the greater circulation.

We are too prone to forget the lymphatic vessel as a route for infection.

*Cerebral Hemorrhage.*—Hemiplegia may occur antepartum, intrapartum, shortly postpartum, or some days after delivery. Hemiplegia occurring during the second or third weeks postpartum is almost always due to infection; later, and even during the first week postpartum, it may be due to infection.

<sup>1</sup> Siemerling, Döderlein Hand. des Geburt., Band 2, S. 467.

<sup>2</sup> Daels, Lequeux and Chome, Gynec. et Obstet., Par., 23, viii, 423.

<sup>3</sup> Rossier, Lequeux and Chome, Gynec. et Obstet., Par., 23, viii, 423.



In the first three classes we think of old or recurrent endocarditis giving rise to embolism. Distinct mitral disease, especially stenosis or a history of acute rheumatic fever or chorea, are very suggestive. Causes for defective blood-vessels must be borne in mind—lues, nephritis, and eclampsia.

In those with defective vessels the straining of parturition may play a part, but probably not so large a one as was formerly thought. In normal labor the uterine contractions probably have but little influence on the blood-pressure, the straining of the general musculature has more. Schwarz<sup>1</sup> in 80 normal cases found a rise of 10 to 20 mm. mercury toward the end of labor; the first ten minutes after delivery the previous level was reached. In some the variation was 40 mm. mercury. But the elevation and fluctuations of blood-pressure in eclampsia are decidedly different. Bailey<sup>2</sup> found a fall of 100 mm. mercury when the uterus was rapidly emptied leading to syncope and if not combatted to shock. The same difference holds true in cesarean section—in normal cases there is no marked drop, in eclampsia a rapid drop of 100 mm. mercury or even more. If the patient is in the later years of child-bearing and the vessels suggest degenerative changes, there is greater danger of hemorrhage, especially if she is at all suffering from kidney insufficiency and even mild eclampsia. Necropsies in eclamptic cases frequently show punctate or even large hemorrhages. Goldberg<sup>3</sup> found that during labor edema is wanting in 50 per cent. of eclamptics; in 10 per cent. of these albuminuria is lacking; after birth albumin is wanting in 12 per cent. and in one to two days after labor in 23 per cent. of eclamptics. The attacks following delivery are more apt to lack uremic symptoms. The hemorrhage and palsy develop usually in close relationship to convulsions. In these eclamptic or albuminuric palsies hemorrhage is not always the basis; transient congestion and edema of the brain sometimes give origin to the so-called "serous apoplexies," whose symptoms fluctuate and improve so rapidly that they may be thought hysterical.

<sup>1</sup> Schwarz, Amer. Jour. Obstet. and Gyn., 6, 656, December, 1923.

<sup>2</sup> Bailey, A. J., Obst., 1911, 64, 260.

<sup>3</sup> Goldberg, Döderlein Hand. Geburt., Band 2, S. 467.

Occasionally varices are responsible for these hemorrhages. Pfannenstiel<sup>1</sup> usually found hemorrhages in eclamptics punctate to the size of a pigeon egg, but one case had a large hemorrhage following the eighty-first convulsive seizure on the eighth day of the eclampsia due to varix in the brain. Others report occasional varices in the veins in the great ganglia as source of the hemorrhage in these cases.

Hemorrhage from the choroid plexus is also described. A friend recently related such a case; there was a large hemorrhage from an apparent varix in the plexus. The writer saw one some time ago in a young woman who was stricken with sudden unconsciousness, stiff and retracted neck, and bloody spinal fluid. She died in a short time; the autopsy showed a ruptured choroid, with the lateral ventricle filled with clotted blood. The hemorrhages may be multiple. Greenacre<sup>2</sup> has made some valuable observations on this subject, though not in puerperal cases. In multiple spontaneous hemorrhages pontine hemorrhage was found secondary to extensive hemorrhage into the internal capsule and the basal ganglia in the majority of cases. The pontine arteries are small, short, terminal branches, given off at nearly a right angle from a large trunk, thus easily involved in any disturbance of circulation in the main trunks.

This may help explain some of the crossed palsies found in some of our cases, especially left-sided palsy and aphasia.

If the experimental work of Sabrezés and Marrias<sup>3</sup> stands the clinical test it will be valuable in differential diagnosis. They draw attention to the occurrence of massive albuminuria without casts in the urine in cerebral hemorrhages.

*Brain Abscess.*—The disintegrating brain infarct simulating abscess has already been mentioned.

A genuine brain abscess causing puerperal hemiplegia would usually be a part of a frank puerperal septicemia.

A marked anemia due to severe postpartum hemorrhage may be one of many factors leading to puerperal hemiplegia, like

<sup>1</sup> Pfannenstiel, *Centralblat. für Gynæk.*, No. 38, S. 601, 1887.

<sup>2</sup> Greenacre, *Bull. Johns Hopkins Hosp.*, 28, 86, February, 1917.

<sup>3</sup> Sabrezés and Marrias, *Paris Presse Medicale*, 1923, xxxi, 104.

the sluggish circulation following delivery, but neither alone nor combined are they sufficient to stand as a sole etiologic factor.

**Physical Signs and Symptoms.**—*Thrombophlebitis.*—A gradual progressive, prolonged increase in pulse-rate is present in about half the cases.

There may be slight fever or a subfebrile temperature. Hans Michaelis holds that a persistent subnormal temperature, postpartum, should make one consider the possibility of thrombosis or embolism. Surely the persistence of a slight elevation of temperature with no explanation in sight indicates this possibility even more strongly. Pain in the groin or leg is probably a late symptom, showing occlusion is beginning. Thrombosis of uterine and pelvic veins shows few if any significant symptoms during life.

Embolism, pulmonary more often, may be the first evidence of its existence. The greater number occur among primipara, especially those who have had operative help in delivery.

*Cerebral thrombophlebitis* may be slow in development and show prodroma, headache, paresthesia in the fingers of one hand, one extremity, or a side; difficulty in speech, paresis in the faciohypoglossal region, or in a hand. Sometimes blunted or lost consciousness is first noticed. Frequently the chief symptom, hemiplegia, is an early one. Preceding this there may be convulsions, local or general, depending upon the extent of the cerebral surface affected by the extravasated blood.

Aphasia, common with right-sided, may occur with left-sided hemiplegia. Recurring vomiting, fever, and increased pulse are quite common. The urine may or may not contain albumin and casts. Stupor may alternate with a state in which the patient is noisy, restless, and irrational. The spinal fluid may show numerous red blood-cells and white blood-cells.

A terminal coma is common and those who succumb usually do so during the first week following development of palsy. Some recover entirely, some with a partial palsy.

*Puerperal pulmonary embolism* is the commonest cause of death during the puerperium when definite disease is lacking. The source of the emboli is more often in the pelvic veins than

the femoral. Usually this phlebitis is latent. An unsuspected endocarditis has been the source of emboli at autopsy. Occasionally we find recorded pulmonary embolism and cerebral embolism with hemiplegia in the same case. Some of the cases thus reported causing puerperal palsy belong to the rheumatic group. Some of the transitory aphasias and partial hemiplegias and monoplegias are probably due to very small emboli, others to eclampsia. In either case they may simulate hysteria. Barrett<sup>1</sup> records a case with apparent cerebral embolism and hemiplegia following a pelvic operation. The patient lived forty-two days. At the autopsy they found pulmonary embolism and edema of the brain, but no cerebral embolism.

*Puerperal Cerebral Hemorrhage.*—The onset is sudden, headache common, and fever is rare. Hemiplegia or convulsions may open the scene, the latter when the blood invades the ventricles or spreads over the cerebral surfaces. Crossed palsy is not rare, so palsy of the lower part of the face and aphasia may accompany the hemiplegia, whether right or left. Hemianesthesia is recorded occasionally. The hemorrhages occur more often in the cerebral ganglia, they may be multiple, one larger and others smaller. Especially on the superficial brain surface the hemorrhage is often really an extravasation due to thrombosis. Few cases are studied carefully enough to distinguish the two. Hunt's<sup>2</sup> cases are models in this respect. The occasional varices in the vessels of the great ganglia have been mentioned. Puerperal thrombosis of both choroidal veins is remarked by Adami and Nichols.<sup>3</sup> The serous apoplexies of kidney disease and eclampsia may arise and give the same picture as true hemorrhage.

**Differential Diagnosis.**—To decide that puerperal hemiplegia is due to cerebral thrombophlebitis, embolism, hemorrhage, or serous apoplexy is difficult if not impossible. In cerebral thrombosis the presence of a known phlebitis is suggestive. Ordinarily the palsy is usually less brusque than in hemorrhage or

<sup>1</sup> Barrett, Canad. Med. Assoc. Jour., 14, 129, February, 1924.

<sup>2</sup> J. H. Hunt, Bull. Lying-In Hosp., 11, 73, May, 1917.

<sup>3</sup> Adami and Nichols, Principles of Pathology, vol. 2, 563.

embolism. There may be the antecedent headache, slight fever, accelerated pulse, paresthesia, paresis, and aphasia. The hemiplegia is, on the whole, slower of development.

Embolism, like hemorrhage, is brusque. The presence of a phlebitis, known or suspected, or of an endocarditis, especially mitral, are more than suggestive. Left-sided occlusion with right-sided hemiplegia is more often due to embolism.

Cerebral hemorrhage is sudden, the palsy complete early. Diseased vessels, as in lues and nephritis, are suggestive. In eclampsia the presence of nausea, vomiting, visual disturbances, edema, albuminuria, if present, are all helpful. The palsy due to cerebral congestion or edema in this connection may be transitory or changeable.

**Prognosis.**—The prognosis, like the symptoms, varies with the underlying cause. The underlying causes differ only that in puerperal hemiplegia we probably always have infection at work. That the thrombophlebitis is always mycotic seems most likely, but that there is a variation in the virulence of the bacteria present seems the rational explanation of the various clinical conditions encountered. Puerperal hemiplegia is grave, but not hopeless. The number of recoveries slightly exceeded the deaths, and but a few of those living had permanent palsies left, and even those show improvement. The permanent disability was never so great as the initial palsy.

**Treatment.**—As far as the local thrombophlebitis is concerned this is largely an obstetric question well handled in any good text-book on the subject.

After forty years of asepsis and its dramatic effect in reducing childbed fever, it seems unbelievable that any accoucheur could neglect this lesson. But we have met the individual who "never uses surgical gloves and never has an infection." Unfortunately the young woman concerned died of virulent septicemia. The lack of gloves was probably but an index of an entire lack of aseptic technic. Infections will happen in the hands of the most skilful and careful, especially where obstetric operations are necessary, as it did in the case of puerperal hemiplegia we add to the list. For the careful obstetrician there is the com-

fort of the observations of Williams. He has seen phlegmasia develop where the woman had never been vaginally examined and in whom the first elevation of temperature occurred in the third week postpartum, also in the second half of pregnancy in an apparently normal woman.

In these manipulation-mad days it behooves the practitioner to see that his treatment is the only one carried out. For nowhere is massage and manipulations more contraindicated than in phlegmasia. Detachment of fragments and consequent embolism is a real danger. On account of the palsy the tendency to use massage is greater and the bad effect on the phlegmasia may be overlooked.

## CLINIC OF DR. HENRY K. MOHLER

JEFFERSON MEDICAL COLLEGE

### DIGITALIS

#### **A Discussion of Its Untoward Effects, of Conditions Under Which it Either Fails to Act or Produces Unfavorable Results.**

OUR knowledge of cardiac disorders has advanced greatly within recent years. We owe this rapid progress mainly to the use of graphic methods interpreted in connection with previously recorded clinical observations and studies.

Some of the problems which baffled physicians have been answered by the polygraph and electrocardiograph, and doubtlessly with the continued interest in this subject much will be added to our knowledge of these disorders.

With the recognition of the nature of many of the cardiac disturbances great advances have been made in their treatment.

In no branch of medicine is careful and skilful treatment of so great importance, and in few are the physician and patient so well rewarded. Digitalis, properly used as one of the general therapeutic measures, has accomplished most unexpected and brilliant results. Literature and experience abound with instances in which digitalis has afforded the greatest relief in cases of heart failure. In the vast majority of instances cases of auricular fibrillation with rapid heart rates show the greatest improvement.

It is my purpose today not to point out or particularly emphasize the good effects of digitalis with which you are already so familiar, but to direct your attention to its untoward effects and to the instances in which it either does not act or produces unfavorable results.

The extraordinary difference in the results obtained from the use of digitalis often is difficult to explain. Different patients complaining of like symptoms and suffering from identical heart lesions respond to digitalis in a most variable manner.

The special indications for the administration of digitalis are a pulse-rate continuously in excess of 85 per minute, loss of contractile force of the heart muscle, resulting in dilation with visceral congestion and edema. Occasionally a heart with a normal rate or little increased above normal will be benefited by digitalis.

The rapid heart-rate, noted in neurocirculatory asthenia and in hyperthyroidism, not only is not benefited by digitalis administration, but accompanying symptoms are often aggravated. In neurocirculatory asthenia, when digitalis is used, the picture may be complicated by the introduction of extrasystoles, increase in precordial pain, and a complaint of more forcible heart action. The extrasystoles, as is the rule, occur more frequently when the patient is at rest, upon retiring, or after a meal, and consequently interfere with his rest. In addition, the occurrence of extrasystoles and of forcible heart action may result in the patient's "starting" in his sleep, and complaining of attacks of dyspnea.

The tachycardia of hyperthyroidism is probably not benefited unless it be due to auricular fibrillation. Cases of similar severity of thyroid intoxication treated by absolute rest in bed with or without digitalis seem to do quite as well. The use of digitalis has not been of any uniform value in the treatment of paroxysmal tachycardia unless the duration of this disorder has inaugurated or aggravated a myocardial failure.

The heart failure seen in postoperative surgical infections, especially acute peritonitis, is seldom benefited by the administration of digitalis. The successful treatment of the surgical factor is usually of greater value in the recovery of the patient than the administration of digitalis. The intravenous use of digitalis under these circumstances is especially dangerous because of the possibility of full doses producing the condition which is usually fatal, viz., ventricular fibrillation.



Patients who suffer from attacks of angina pectoris and who are treated with the usual dosage of digitalis during the interval of the attacks, are often made worse. Not only may the attacks last longer, but they may increase in number. Recent investigations indicate that angina pectoris frequently occurs without any impairment of the integrity of the heart muscle, the lesion being in the aorta.

In the form of cardiac irregularity known as sinus arrhythmia digitalis is without effect and may produce extrasystoles and more forcible action of the heart and even partial heart-block. This form of irregularity occurs in the young and in older persons who have an unstable nervous system, and requires no treatment for the heart. The pulse-rate increases with inspiration and slows with expiration with no evil effects upon the body.

The most common form of irregular pulse-rate seen in apparently healthy adults is that due to extrasystoles. In a number of instances the patient has not been aware of a "dropped beat" or a "missed beat" until so informed by the physician. This form of irregularity needs no treatment of the heart muscle unless other physical signs or symptoms are present indicating failure of the myocardium, and is either not benefited by digitalis or is made worse by its use.

Partial heart-block, a condition in which the ventricles fail to respond to every second, third, or fourth auricular contraction, may be converted into a complete block by the use of digitalis. During the period of conversion from a partial to a complete block and before the ventricle has taken on its own rhythm, syncopal attacks may occur.

In auricular fibrillation digitalis may fail to produce a good result if the pulse-rate be taken as the guide rather than the heart rate. Digitalis, if it is used in the treatment of this disorder, to be most effective must lower the heart to a range of 65 to 75 per minute. The heart-rate of 70 per minute in auricular fibrillation because of weak or imperceptible beats at the wrist, may yield a radial pulse of but 40 to 50 per minute or, expressed in other words, a pulse-rate at the wrist of 70 per minute may be

accompanied by a heart-rate of 90 or more, a condition referred to as a pulse deficit. Digitalis may, therefore, fail to relieve the patient if the radial pulse-rate is reduced in frequency to 70 per minute, having neglected to use the heart-rate (determined by auscultation) as a guide. When the contractile power of the heart muscle is exhausted, digitalis may slow the pulse-rate of auricular fibrillation to within normal range, but with no improvement in dyspnea, edema, and other accompanying symptoms.

Cases of auricular fibrillation with heart failure and slow pulse-rates are usually not benefited by the administration of digitalis. The failure is due to the extreme poor state of myocardium and predicts an early, unfavorable result.

There exists considerable difference in opinion as to whether digitalis benefits cases of heart failure, in which the pulse-rate is regular. There seems to be sufficient evidence that digitalis benefits many cases of heart failure with a regular pulse. Unquestionably there are instances of heart failure which have been treated by rest, and when digitalis has been added to the plan of treatment further improvement was noticed which could only be ascribed to the use of digitalis. Small doses under these conditions are safer and yield better results. The danger of giving larger doses in cases of myocardial degeneration with areas of softening or fatty degeneration is to produce a rupture of the heart.

Disappointment is often experienced in the intravenous use of digitalis in cases that appear to be heart failure. Sudden interferences with the coronary circulation is accompanied by acute precordial pain and symptoms of heart failure. The use of digitalis under these circumstances is usually of no value and may produce ventricular fibrillation, a condition which is usually fatal and frequently present in preagonal states.

**Improper Administration and Dosage.**—Digitalis fails to act or its action is delayed because the dose is too small or it is not absorbed. If considerable edema is present, absorption from the alimentary tract, when digitalis is given orally, and from edematous tissue when given subcutaneously, is very much de-

layed, and occasionally intravenous methods may be necessary to produce effects within several hours.

When the symptoms are urgent the drug should be given so that the adult patient absorbs from 4 to 8 c.c. of the tincture within twenty-four hours.

Digitalis often fails when its administration is continued too long or when the dosage is too large. In auricular fibrillation, if digitalis is continued over too great a time or the dosage is too large, "coupling of the beat" may be produced, and the patient complains of precordial distress, dyspnea, fulness in the head, and syncopal attack or vertigo.

In all instances of benefit by digitalis, if its administration is continued to the point of poisoning, the following symptoms may develop—nausea, vomiting, diarrhea, headache, and diminution of vision.

Failure to obtain results from digitalis administration may result because poor preparations of digitalis are supplied. Either the drug is inactive or the preparation made therefrom does not contain the active principles of digitalis. Modified digitalis preparations, about which the profession has no knowledge as to the composition or strength, are dangerous to use, especially those designated for intravenous use. Tincture of digitalis, or the powdered digitalis leaves, physiologically assayed, have produced the best results by oral administration.

For subcutaneous or intravenous injection suitable preparations of digitalis are manufactured, but one should be familiar with their action before too much reliance is placed upon them. Tincture of digitalis is more effective when administered in the uncombined form, that is, not in combination with other drugs.

Digitalis usually will not act effectively in the presence of fever. Hare, in a verbal communication, states that the use of digitalis in some cases of pneumonia is attended with grave consequences. He states that the pneumonia toxin acting upon the auriculoventricular bundle may interfere with the transmission of the auricular impulse, and that digitalis further decreasing the conductivity of this structure may produce varying degrees of heart-block.

The heart of diphtheria patients should be very carefully studied before digitalis is used, lest distressing symptoms may result.

Digitalis has been credited with having a cumulative effect, but the danger is probably not as great as it was thought to be. The sudden disappearance of extensive edema, when digitalis has been taken over a long period of time, may result in the rapid absorption of the drug, producing symptoms of digitalis poisoning. Such action is not frequent.

Digitalis, as are many other drugs, is at times not tolerated by certain individuals, even though the use of the drug is strongly indicated. This peculiar action may only be explained by stating that the patient has an idiosyncrasy for this drug. Other members of the digitalis group should therefore be employed.

This discussion is not intended to discredit the use of one of the most valuable drugs at the command of the medical profession, but rather to emphasize the need for the careful study and examination of the patient and the drug before condemning it, especially if administered when it is either contraindicated or under conditions that it is not capable of producing beneficial results.

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**INSULIN IN DIABETICS REQUIRING SURGERY**

PRIOR to insulin the prognosis for all diabetics requiring surgical assistance was poor, but by the proper use of diet and insulin the usual percentage of success as for non-diabetics can now be predicted.

We have had a small series of diabetics requiring operations under the following conditions:

1. Carbuncles (3).
2. Perforating ulcer of toes with bone necrosis (5).
3. Severe palmar abscess (1).
4. Gangrene of foot and leg requiring amputation (7).
5. Otitis media and mastoiditis (3).
6. Strangulated hernia (1).
7. Intestinal obstruction (1).
8. General peritonitis from ruptured appendix (1).
9. Ischiorectal abscess (2).
10. Tonsillectomies (7).

In the series of amputations of the leg there were 3 fatalities. We will first give a brief review of the fatal cases:

Our first death in a diabetic requiring surgery was a woman aged seventy who was markedly emaciated and had a definite advanced arteriosclerosis. No pulsation could be detected in the dorsalis pedis or posterior tibials of either foot. There was an area of dry gangrene 9 x 11 cm. on the dorsum of the right foot. Her blood-pressure was 182 systolic, 96 diastolic, blood-sugar 400 mg. per 100 c.c. of blood; all of the above present on

admission. Diet and insulin reduced her blood-sugar to a satisfactory level. We considered her a mild diabetic, but the area of gangrene continued to extend, and on the thirty-seventh day after her admission to the hospital it was decided to amputate her leg. This was done at the middle third of the femur under nitrous oxid oxygen anesthesia. Postoperative progress unfavorable. The flaps became gangrenous, then infected, and then new areas of inflammation and infection developed on the buttocks, hips, elbows, back, and even on her ears. Her insulin requirement gradually increased to 100 units daily. She died sixty-nine days after admission of generalized sepsis.

Mr. M., Hospital No. 29,188, aged seventy-five, emaciated, marked arteriosclerosis, arteries definitely beaded. No pulsations could be felt in arterial supply of left foot. Right foot had been amputated three years before on account of gangrene. Glycosuria detected at that time. Left foot at time of admission had perforated ulcer involving distal phalanx of great toe. x-Ray report of left foot was as follows: "Shows arteriosclerosis of vessels with osteoporosis of the bones of foot and osteitis in distal phalanx of great and second toes." Insulin and diet controlled diabetes ideally, but the diseased toe did not respond and gangrene of toe finally developed. The visiting surgeon considered the gangrene of the senile type. Finally, three months after admission, the great toe was amputated. Following amputation of toe moist gangrene rapidly developed and soon involved leg. Three days after operation on toe consultants decided to amputate above the knee. Patient did not do well and died two days later with high temperature and evidence of sepsis.

Mrs. B., Hospital No. 29,517, age fifty-nine years, obese, arterial thickening increased for her age. Blood-pressure 168 systolic, 88 diastolic. Heart: No murmurs, but a mild heart-block was present. Extremities: There was dry gangrene over entire left foot including ankle, and moist gangrene over upper third of leg with much inflammation and no line of demarcation.

Known duration of diabetes about one month. Patient admitted to hospital about 10 P. M. with septic temperature and blood-sugar of 270 mg. per 100. Preparatory diabetic emergency treatment instituted and leg amputated under local anesthesia at 7.30 A. M. next morning. Returned to her room in good condition. Blood-sugar 150 two hours after operation. Patient did well during the day. At 2.50 A. M. special nurse's records show her respirations 20 and pulse 100 per minute. At 3 A. M. she made a deep respiratory effort and ceased breathing. Autopsy not permitted.

We had one other death following surgical interference in a case with perforating ulcer of toe and osteomyelitis of metatarsal bones. Mrs. S., Hospital No. 29,517, aged sixty-nine years. She had been admitted to hospital in December, 1923, with severe diabetes. She responded to treatment and was discharged from the hospital with insulin dosage and diet perfectly balanced. Her history shows that about one month after leaving the hospital the left little toe became sore and foot swollen. This toe later discharged pus. Patient continued under care of family doctor until May 13, 1924, when she was readmitted to Memorial Hospital. Her left little toe was gangrenous and foot swollen and discolored. x-Ray report: "Osteomyelitis of proximal, middle and distal phalanges, and distal metatarsal bone of little toe." Patient operated on under local anesthesia on May 15th. Little toe and metatarsal bone removed. Surgical wound did well for ten or twelve days, when foot became swollen and painful. No definite areas of fluctuation could be detected, but it was decided to incise an indurated inflamed area below the external malleolus. No collection of pus was found. The next day patient had a chill and temperature reached 103° F., lungs normal, white blood-count 33,200. Blood-culture taken 6/3/24 showed streptococcus. Patient rapidly grew worse and died with blood-sugar of 91 on 6/6/24.

These cases all had normal blood chemistry for some time prior to their deaths. Since autopsies could not be procured,

especially on the amputation cases, no definite statement could be made as to cause of death. Two of the leg amputation cases had the senile type of gangrene and the diabetes was probably due to the generalized arteriosclerosis involving the pancreas. In such cases we are of the opinion that amputation hastens death and is therefore contraindicated.

We will report in detail a few of the successful cases:

William H.; diabetes with gangrene of right foot and leg. Duration five years. Nine months before admission to Memorial Hospital an ulcer appeared on the little toe of the right foot which soon became gangrenous and, although dry, gradually extended. At the time of admission there was involvement of all the toes and the foot as far back as the middle of the metatarsals. Moist gangrene extended to the middle third of the leg and a diffuse inflammatory cellulitis to the knee-joint. Patient complained of constant, severe pain. His temperature was 101.4° F., pulse 132. Laboratory findings:

Urine: acid, 1.021; alb. plus, gluc. 2 plus, acetone negative.

Blood-urea nitrogen—14 mg.

Plasma blood-sugar—281 mg.

Blood Wassermann negative.

Slight secondary anemia; no leukocytosis.

Patient was admitted late in the afternoon and was immediately given 14.5 units of insulin followed by 10 gm. of carbohydrates. This was repeated at midnight and the blood-sugar at 8 A. M. next day was 147; 14.5 units more of insulin with 10 gm. of carbohydrates were then administered. He was operated upon at 12 M. under nitrous oxid oxygen anesthesia, the leg being amputated at the upper third of the thigh. Operation completed at 1.20 P. M.

Blood-sugar immediately before operation, 185 mg.

Blood-sugar postoperative, 235 mg.

(Showing an increase of 50 mg. even when gas and oxygen anesthesia was used.)

14.5 units of insulin administered at 2.35 P. M.

14.5 units of insulin administered at 5 P. M.



14.5 units of insulin administered at midnight.

Carbohydrates were administered after each dose of insulin. The patient had a good night, temperature normal the next morning after operation, and remained so throughout his convalescence. Blood-sugar morning following operation 285 mg. For several days he was given 58 units of insulin daily, with a food intake of 1800 calories. His insulin dosage was gradually decreased to about 36 units daily and his blood-sugar ranged between 117 and 133. Surgically he did as well as a non-diabetic patient, wound healed by first intention, and patient feeling happy and free from pain. Recovery in such cases is impossible without insulin. William H. was discharged October 13, 1923; present dose of insulin 26.5 units per diem; diet 1856 calories. This patient's comments were: "They tried for nine months to get me in condition for operation and failed; with insulin you got me ready in nine hours."

**Strangulated Incisional Hernia.**—Patient, Mrs. X., was referred to us by Dr. Edward A. Parker, of Philadelphia, after an emergency operation for an incisional strangulated hernia. She gave a history of diabetes of six months' duration, so the surgeon wisely used nitrous oxid oxygen anesthesia, requiring 30 mils. of ether. The following is Doctor Parker's description of operation:

"Patient anesthetized with nitrous oxid and oxygen requiring only 1 ounce of ether for complete muscular relaxation. Midline incision slightly to the left of previous scar. Muscle separated in the linea alba. Hernia sac dissected over the fascia of external oblique muscle to a point near the anterior superior spine of the ilium. The entire sac split transversely. The pyloric end of the stomach and the first 4 feet of bowel and omentum which occupied the sac were matted together by dense fibrous adhesions which were not disturbed. At points where the bowel and omentum adhered to the sac wall the adhesions were broken up. The contents were returned to the abdominal cavity and the neck of the sac cut across at a point where it emerged from the ring in the fascia. The hernial sac was not dissected out, but simply packed with gauze. The peritoneum was closed with a continuous No. 0 chromic catgut suture. The fascia was imbricated and closed with a continuous mattress-suture. All sponges and instruments were accounted for. Skin was closed by interrupted silk-worm-gut sutures. Patient reacted well to operation."

Operation completed at 1.50 P. M. Patient soon recovered consciousness, but went into coma about 2.30 P. M. I saw her at 3 P. M. She could not be aroused; vomiting; incontinence of urine and feces. The chart below gives blood-sugar and insulin dosage:

DATE	TIME	BLOOD SUGAR	INSULIN	REMARKS
9-11-23	3 <sup>05</sup> PM	277	20	PATIENT UNCONSCIOUS VOMITING
9-11-23	7 <sup>00</sup> PM	266	30	CONDITION UNCHANGED
9-11-23	11 <sup>00</sup> PM	235	50	MARKED IMPROVEMENT
9-12-23	1 <sup>00</sup> AM		30	CONSCIOUS VOMITING CEASED.
9-12-23	3 <sup>00</sup> AM		30	
9-12-23	7 <sup>00</sup> AM	70		
9-12-23	9 <sup>00</sup> AM	98		
9-12-23	1 <sup>00</sup> PM	186	10	
9-12-23	5 <sup>30</sup> PM		30	
9-12-23	7 <sup>00</sup> PM	129		
9-13-23	8 <sup>00</sup> AM	200	20	

INSULIN DOSAGE ON THIS CHART "H" UNITS.

The urine was positive for glucose, and gave strong ferric chlorid reaction. I regret that a plasma CO<sub>2</sub> and other chemical evidences of acidosis were not obtained. As my resident physician and I had every minute occupied with blood-sugar estimations, intravenous saline and glucose, in addition to the general supervision of patient, further laboratory work was impossible. At 1 A. M. vomiting had ceased, patient was conscious, and taking liquids by mouth. Three days after operation insulin was discontinued and her diabetes was controlled by diet. The operative wound united by first intention and her convalescence was as uneventful as that of a non-diabetic.

**Infected Finger and Palmar Abscess.**—Dr. O. F., patient admitted to Memorial Hospital May 23, 1923. Known duration of diabetes one month. Obese, weighing 214 pounds—at least 50 pounds over his ideal weight. A diet of 30 calories per kilogram of body weight, arranged to give the proper keto-antiketogenic ratio, soon corrected glycosuria and hyperglycemia. After mastering the prescription diet he was discharged with normal urinary and blood-sugars, weighing 174 pounds, and was satisfied with the results obtained.

On August 11, 1923 patient accidentally cut off the end of his left ring finger, just back of the matrix. He was admitted to the hospital next day to have the end of bone removed in order that the proper flap could be formed. He insisted upon a general anesthetic and nitrous oxid and oxygen was used. Blood-sugar before operation was 108, after operation 133. He required 7 units of insulin daily to keep his urine sugar free and blood-sugar below 130 mg. per 100 c.c. of blood. By the third day a severe infection had developed in the injured finger and the insulin dosage was increased to 10.5 units per day. Later a palmar abscess formed, requiring several operations. The duration of the palmar infection was eight weeks. During this time his insulin dosage reached as high as 23 units daily. As the infection subsided the insulin dosage was reduced until October 28th, when his urine being sugar free and blood-sugar normal, no insulin was administered. Since that date the urine and blood chemistry have been normal, his physical and mental efficiency 100 per cent., and weight 164 pounds. He follows faithfully his diet of 30 calories per kilogram of body weight; a living example of the value of insulin and diet for those diabetics requiring surgery. This and also the case of strangulated incisional hernia conclusively negatives the statement frequently heard "once use insulin, always use it."

A case of diabetic coma operated upon for intestinal obstruction. Hospital No. 29,221, a boy of thirteen years, fairly well nourished, unconscious when admitted to the hospital, the family physician's diagnosis being intestinal obstruction. The following history was obtained from family physician:

for several days prior to admission child had felt tired and weak, two days before hospitalization began vomiting, had pain in stomach, bowels regular. His physician administered morphin and finally sent child to hospital in the evening with a diagnosis of intestinal obstruction and peritonitis. The admitting physician sent patient to surgical ward and recorded the following observations: "Tenderness in right abdomen with great rigidity, also fluid in abdomen." These observations, however, were not confirmed by the surgical resident physician who also examined patient immediately after admission. He found rigidity only during the act of vomiting, and after the report of his urine examination showed a heavy cloud of albumin, rapid reduction of Benedict's solution and marked reaction to the ferric chlorid test, the surgical resident made a diagnosis of diabetic coma. However, the diagnosis of the family physician was accepted, the child was immediately taken to the operating-room, but the medical resident was given permission to take blood immediately before operation for a sugar estimation. Those adhering to the "surgical abdomen" diagnosis justified their diagnosis by the history of vomiting, pain in abdomen, and leukocytosis of 15,500 which the blood-count revealed. The points influencing them in such a decision were a history of abdominal pain, vomiting, and a leukocytosis. All these are present in a surgical abdomen, but they may also be present in severe diabetic acidosis, especially the leukocytosis, which frequently is above 40,000. Thirty minutes' delay for a blood-sugar estimation would have given definite data for a correct diagnosis. Ether anesthesia was used. The surgeon reported no fluid in abdomen, no peritonitis, but several small incisions about  $\frac{1}{2}$  inch in length, with no inflammatory reaction. These were easily reduced and the abdomen closed after inserting 500 c.c. of saline in peritoneal cavity. By this time blood-sugar estimation was completed and revealed 960 mg. of glucose per 100 c.c. of blood. This, of course, was a preoperative specimen. Patient was sent to diabetic ward at 10.30 p. m. and 30 units of insulin given intravenously, immediately followed by 20 units subcutaneously. Alveolar  $\text{CO}_2$  estimation at this time was 10.

Patient was also given 500 c.c. of saline by hypodermoclysis and proctoclysis was started. As the pulse was rapid and irregular and blood-pressure 84 mg. of mercury, he was given 10 minims of tincture of digitalis hypodermically every three hours. His blood-sugar at 11.30 P. M. was 769 mg. and plasma  $\text{CO}_2$  10.7, so we repeated the 50 units of insulin as above. At 12.10 A. M. he was given 30 units of insulin intravenously and 20 hypodermically. At 1.30 A. M. blood was taken for a glucose estimation and 50 units of insulin administered as previously. This blood specimen showed a blood-sugar of 645 mg. At 4.30 A. M. blood-sugar had been reduced to 363 mg. and he was given 40 units, 20 intravenously and 20 hypodermically, also 500 c.c. of saline by hypodermoclysis. At 7.15 A. M. his blood-sugar was 246, pulse better, respirations more normal, and he was at this time given 20 units of insulin hypodermically. At 9.30 A. M. consciousness returned, patient could talk rationally, and also swallow liquids. On account of the laparotomy he was given only liquids during the day, receiving 60 grams of carbohydrates in the form of orange juice and 40 units of insulin up to 10 P. M., when his blood-sugar was 125. This patient, aged thirteen, weight about 80 pounds, was given 260 units of insulin from 10.30 P. M. to 7.15 A. M. the next morning, when his blood-sugar was 246 mg. per 100 c.c. of blood. He was given no carbohydrates and no alkalis during this time. He was admitted to the hospital March 8, 1924, and for several months he has been consuming daily 1700 calories and has required only 5 units of insulin daily to keep him in perfect balance, and since the first of June he has been performing all the activities of a healthy robust boy of his age. This case fortifies us in the opinion that the degree of acidosis is the determinant of insulin dosage in coma, also that cases in deep coma must be given so-called heroic doses of insulin frequently repeated and carefully controlled by blood chemistry, and also suggests the advisability of administering fluid intraperitoneally to overcome desiccation. This method is especially adapted to children whose veins are so small that intravenous administration is difficult if not impossible.

The space allotted us will permit the brief mention of one

other operative case, and we selected the following one because we believe it shows the impairment of the internal secretion of the pancreas in units of insulin in this special case by a severe general peritonitis:

Patient, H. E., Hospital No. 29,952, admitted to Memorial Hospital March 1, 1923, with a moderately severe diabetes of many years' duration. He was discharged April 3, 1923, on a maintenance diet of 30 calories per kilogram of body weight requiring 25 units of iletin daily, his blood-sugar ranging from 110 to 150 mg. and urine sugar free at all times. Upon this diet and insulin dosage he led an active life and resumed his former business until March 22, 1924, when he was admitted to the hospital with a ruptured gangrenous appendix and severe general peritonitis. Operation was immediately performed and abdomen drained. Postoperative progress ideal. We kept him in the hospital ninety-one days hoping to reduce his insulin requirements to the 25 units which he required prior to his peritonitis. This, however, we could not accomplish, and he was discharged on the ninety-first day after admission consuming 30 calories per kilogram, requiring 55 units to keep him sugar free and his blood-sugar within the limits of normal. Six months after operation he still requires 55 units of insulin daily, showing an impairment of the internal secretion of the pancreas of 30 units of insulin. Since there are no physical or laboratory evidences of a focus of infection it seems fair to assume that his attack of peritonitis is the cause of the lessened function of the pancreas, and this lessened function measured in units of insulin shows 30 units of a reduction.

We would like to record our views at this time in regard to a focus of infection influencing the dose of insulin. We feel that any patient requiring over 70 units of insulin daily has some complication, probably a focus of infection which inhibits the action of the insulin administered, at least this has been our observation in all cases requiring over 70 units of insulin daily. The remark is frequently made that insulin does not work in all cases of diabetes. So far we have found no case that failed

to respond to insulin treatment unless that case had a definite focus of infection. Upon the removal of the infection the insulin had the desired effect upon metabolism. Neither of us are surgeons, but our observations show that the surgical technic in operations upon diabetics does not differ from that used in similar conditions in non-diabetics. This is also the opinion of surgeons with whom we have discussed the subject. Professor John B. Deaver states, "Little, however, can be done without the ready co-operation of the internist and the surgeon. Co-operation between the two is desirable at all times, but at no time more so than in the management of the diabetic. The surgeon, to a great extent, must rely on the judgment and experience of the internist, who has made the study of diabetes and its control his own."

In Memorial Hospital the following plan is routine: Diabetics requiring surgery are either admitted to or remain in the department for the treatment of diabetes. All preparation except local preparation of the area of operation is directed by the chief of the Department of Diseases of Metabolism, and then the patient returns to this Department after operation, the surgeon taking full charge of the seat of operation, the Chief of the Department of Metabolism being responsible for all food and medication. The surgeons and internists of Memorial Hospital agree that in this way only is the danger of diabetes in those requiring surgery lessened.

In addition to the usual surgical preparation the patient should have diabetic preparation. The diabetic preparation if efficiently done requires no more time than the surgical preparation and is equally important whether the diabetes is severe or mild. The surgeons have an emergency surgical preparation and also a routine surgical preparation, and we use an emergency diabetic preparation upon all cases requiring emergency surgery.

**Emergency Diabetic Preparation.**—The emergency diabetic preparation is as follows: A catheterized specimen of urine is immediately examined for glucose and diacetic acid. If the specimen contains glucose and a definite diacetic acid reaction, procure a specimen of blood for glucose and  $\text{CO}_2$  estimation,

these analyses being done in the laboratory during operation, and then immediately administer 10 or more units of insulin, depending upon the glycosuria and the urinary evidences of acidosis before operation.

**Routine Diabetic Preparation.**—This should be instituted a day or two before, as is the ordinary surgical preparation. Acidosis and blood-sugar estimations prior to first meal after admission are made, and if acidosis and hyperglycemia are present administer insulin in proper amounts, estimating insulin effect by blood chemistry within three hours. If the case is a severe one, repeat blood chemistry during the night and administer additional insulin if indicated. Give enemas. Diabetics should not be purged. If not a gastric case, permit patient to take carbohydrates in liquid form and drink water up to one hour prior to operation. Insulin in proper doses immediately before operation if glycosuria or hyperglycemia are present. There is no ideal anesthetic for diabetics. If spinal or local anesthesia can be used these should have preference, then nitrous oxid oxygen, ether, and lastly chloroform. Liquids immediately after operation, either by proctoclysis, hypodermoclysis, or intravenously, according to the chemical severity of the case. Patient should receive 1000 c.c. of liquids every six hours. Subsequent insulin dosage is regulated by the chemical data of the patient, and if this shows marked change from normal prior to operation, give 20 units of insulin immediately after operation is completed. The danger time for postoperative diabetics is from three to five hours after the completion of the operation. Blood chemistry studies should be made at this time even if the patient is conscious.

The postoperative treatment of diabetics requiring surgery differs materially from the after-operation treatment of many surgeons. We give carbohydrates and liquids within two or three hours after operation is completed. If oral administration is contraindicated, give glucose intravenously and liquids parenterally, for the only way to prevent postoperative acidosis is by administering carbohydrates, liquids, and occasionally insulin.



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THE DIAPHRAGMATIC PINCH-COCK IN HEALTH AND DISEASE

THE diaphragm is usually regarded solely as an organ of respiration, and by the surgeon as a partition to keep him from

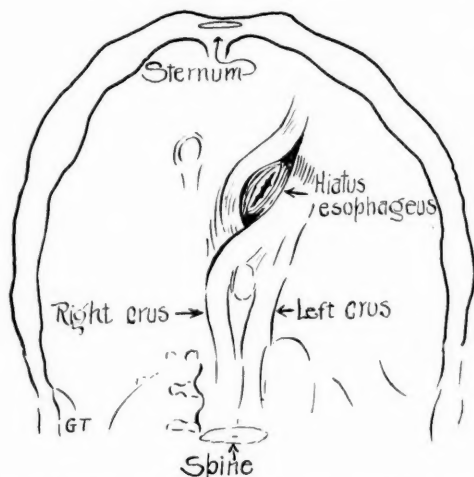


Fig. 147.—Schematic illustration of the under surface of the diaphragm showing the manner in which diaphragmatic tendinous fibers, after diverging from the crura, surround the hiatus to form the diaphragmatic pinch-cock. This is the normal stop-cock against regurgitation of gastric contents, and is the chief factor in the functional group of cases of so-called "cardio-spasm," a disease which is not at the cardia, is not truly spasmodic, and is often organic.

thoracic complications so long as he avoids penetrating it. That it has another and a very important function is not so

generally recognized. Just as the commonly used pinch-cock in the laboratory cuts off the flow of reagents or other fluids through the rubber tube, so does the diaphragm cut off the flow through the esophagus at the diaphragmatic hiatus esophageus. Furthermore, like the laboratory pinch-cock, the diaphragmatic pinch-cock remains tightly closed all the time except when opened. This occurs in co-ordinate response to a peristaltic wave to let a bolus of food pass down into the stomach, or in response to a co-ordinate antiperistaltic wave to permit of emesis. Why does it remain closed all the time by tonic contraction? Let me read to you what Chevalier Jackson has said on this subject: "The pinch-cock action of the periesophageal diaphragmatic structures, especially the sphincter-like prolongations of the crura, with a kinking of the abdominal esophagus, undoubtedly accounts for the fact that a man may stand on his head after drinking a quart of water or eating a full meal without any of the stomach contents gravitating out of the stomach into the esophagus, and, indeed, without the acrobat experiencing any subjective sensation of the mechanism by which the gastro-esophageal communication is so tightly closed to retrograde leakage. More remarkable still is the fact that a man may, with a stomach nominally full of liquid food, assume a position with the mouth much below the level of the stomach, swallow liquids against gravity through an esophagus steeply slanted upward, adding to the fluid in the gastric reservoir without any of the gastric contents escaping. The efficiency of this normal combined pinch-cock and kinking closure against regurgitation is wonderful. In going down the esophagus with the esophagoscope the pinch-cock action is so manifest, and so manifestly at the hiatus, as to admit of no dispute. This pinch-cock action is evidently normal, and evidently, also, it is momentarily relaxed by the co-ordinate deglutitory mechanism with every normal swallowing act and with the somewhat less well co-ordinated act of emesis."<sup>1</sup>

At the cricopharyngeus the esophagus is closed all the time

<sup>1</sup> Jackson, Chevalier, *The Diaphragmatic Pinchcock*, *The Laryngoscope*, January, 1922.

except on swallowing and on vomiting. As at the pylorus, the ileocecal valve, and the sphincter the contents of the alimentary canal normally move one way. As Dr. Jackson has said: "These along with the diaphragmatic pinch-cock constitute a series of check-valves functioning against back flow like the brass check-valves that constitute an indispensable part of every water system."

The particular function of the diaphragmatic pinch-cock is to prevent back flow from the stomach. The best way to see the pinch-cock action is through the esophagoscope. At peroral esophagoscopy it is a tight pucker which yields to gentle but continued pressure on the proper place. At retrograde esophagoscopy in gastrostomized patients it is also a tight pucker, but the shape of the folds is different and the location of the permeable lumen requires a longer search to find it.

We are all, I hope, living examples of the diaphragmatic pinch-cock in health. Now let us consider the diaphragmatic pinch-cock in disease.

Compared to the pyloric duodenal or appendical regions, the neighborhood of the diaphragmatic pinch-cock is not a frequently diseased area; but the esophagoscope has revealed the fact that the lower third of the esophagus including the pinch-cock is a common site of chronic esophagitis, erosions, peptic ulcer, and cancer. The disease miscalled "cardiospasm," which is neither spasmodic nor at the cardia, has its location here or close by. Mosher has shown that many cases of so-called "cardiospasm" are really an organic stenosis of the abdominal esophagus caused by organic abdominal disease, especially disease of the liver. In other cases he has shown the typical syndrome of "cardiospasm" to be really a compression by basic pulmonary disease without any element of spasm.<sup>1</sup>

Chevalier Jackson has suggested the name "ingluviosis" for this syndrome of stenosis at the lower end of the esophagus with dilatation and with trickling of food through the stenotic canal into the stomach. This is the normal physiologic mechan-

<sup>1</sup> Mosher, H. P., *The Liver Tunnel and Cardiospasm*, *The Laryngoscope*, May, 1922.

ism in birds with ingluvies, hence the name ingluviosis. Another name he has suggested is "preventriculosis," because the obstruction is located just ahead of the stomach. Some such name seems necessary since "cardiospasm" is so misleading and is altogether without an anatomic or pathologic basis. An additional reason is that while there are a number of different pathologic mechanisms, organic and otherwise, the condition is a very definite clinical entity. Either of these names describe the pathologic condition present, leaving the final analysis and percentage determination of the various causes to the future.

In the following cases complete and thorough history taking, general examinations, laboratory tests, etc., were carried out to the utmost detail by my colleagues at the University Hospital; but for the present purposes it seems best to omit everything that was negative.

#### **Case I. Compression Stenosis of the Abdominal Esophagus.**

—This woman, aged forty-two years, was referred to the Bronchoscopic Clinic with a tentative diagnosis of cardiospasm. There had been regurgitation of stale fermented food, often foods eaten twenty-four hours before would come up. Hydrochloric acid was absent from the regurgitated material. The condition had come on rather suddenly after an operation at which the gall-bladder had been drained about six months previously. The area of hepatic dulness was markedly increased. On passing the adult esophagoscope nothing to suggest engorged or varicose veins was found. The abdominal esophagus was so small in lumen that the adult esophagoscope would not pass without more pressure than was deemed advisable. The child's size (7 mm. diameter), however, passed through readily into the stomach, though it was apparent that any larger tube would be a tight fit. The mucosa of the abdominal esophagus was normal, as was also the gastric mucosa.

*Esophagoscopic Diagnosis.*—Compression stenosis of the abdominal esophagus.

*Comment.*—This was undoubtedly a case of compression of the abdominal esophagus by the left lobe of the liver, a con-

dition often mistaken for spasmodic stenosis as first pointed out by Mosher. The patient thought her trouble was due to the operation, and one practitioner, who had made a diagnosis of cardiospasm, thought the psychic disturbance had operated as an etiologic factor in the way that often deceptively appears to occur in these cases. It is clear, however, that the compression was the result of the hepatic trouble for which the operation had been done.

*Treatment.*—The treatment of the condition is a problem for the gastroenterologist and the abdominal surgeon. Esophagoscopic dilatation might be tried later if the condition of the liver should prove incurable.

**Case II. Esophageal Stenosis.**—This man, aged fifty-one years, was referred to the Bronchoscopic Clinic from Dr. Stengel's service for esophagoscopy and gastroscopy to determine the cause for regurgitation of blood-stained food. The patient had been told at another hospital, in another city, that he had cancer of the stomach, and that he would not get well without removal of a portion of his stomach. This diagnosis was negatived by Dr. Stengel and his associates.

Dr. Henry K. Pancoast had reported the condition as so-called "cardiospasm" with no Roentgen-ray evidence of malignancy in either the esophagus, stomach, or intestinal tract.

*Gastroscopy.*—On passing the esophagoscope we found a white, pasty, mucosa, ending in a "flat-floor" dilatation at the diaphragm. Locating the hiatal region, we found the esophageal folds eroded and bleeding, the esophageal contents being largely blood with a slight admixture of stale, rancid, cheesy smelling food. This came away automatically in the auxiliary canal of the esophagoscope. Wiping the mucosa revealed the fact that the blood came from superficial erosions in an area of chronic esophagitis. Nowhere was there deep infiltrated ulceration; nor were there any fungations. The esophagoscope went through the hiatus with no more resistance than in case of a normal hiatal esophagus.

I was using the 53 cm. esophagoscope, which is really a gastro-

scope. The tube mouth being then in the stomach, we proceeded to explore this viscus. All of the gastric mucosal area was readily explorable with the exception of the pyloric antrum. The gastric mucosa was found chronically inflamed, but nowhere was there a malignant lesion. Slight erosion existed in the neighborhood of the cardia.

The esophagoscopy and gastroscopy together required ten minutes. No anesthetic, general or local, was used. The patient did not complain of the procedure being painful.

*Diagnosis.*—Ingluviosis or preentriculosis (so-called "cardio-spasm"), chronic static esophagitis with erosions, chronic gastritis. No evidence of malignancy in any portion of the alimentary canal proximal to the pyloric antrum. Source of blood in regurgitated food is esophageal erosions.

*Treatment.*—Weekly applications of chlorlyptus alternated with argyrol were made by peroral esophagoscopy to the erosions in the esophagus and stomach. The diet was limited to unirritating liquids, with an abundance of strained vegetable soups and fruit juices.

*Result.*—Today this man returns to tell us he is perfectly well.

*Comment.*—Here we have a man who before admission had been erroneously and needlessly condemned to undergo the tortures of anticipation of a death by cancer of the stomach. The clinicians and the roentgenologist at the University Hospital had excluded cancer. With the esophagoscope and gastroscope we were able to confirm this exclusion and to contribute materially to the cure of the patient by the dilatation of repeated esophagoscopies and by local applications to local lesions.

## CONTRIBUTION BY DR. SIMON S. LEOPOLD

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### FAMILIAL ARTERIAL DISEASE WITH ILLUSTRATIVE CASE REPORT

It is conceded that there are certain well-recognized causes for arterial and renal disease, the most important of which are: infectious diseases, certain intoxications, and various disorders of metabolism. It is equally true that there are a great many cases where none of these factors may be said to be the cause.

Christian,<sup>1</sup> writing on the etiology of chronic nephritis, states. "If we assume that these infections and infectious diseases do produce chronic nephritis, then it is even more difficult to explain why, in so many people, they occur without producing nephritis; . . . so far as the individual with chronic nephritis is concerned, we can do little more than guess a cause."

Ringer<sup>2</sup> and others express similar views on the etiology of nephritis.

There is another cause of chronic nephritis which deserves emphasis. It is heredity. Kidd<sup>3</sup> in 1882 wrote on the inheritance of Bright's disease, and reported this disease extending through three generations.

A recent article on hereditary and familial nephritis, by Eason, Smith, and Buchanan,<sup>4</sup> cites the occurrence of this disease in several members of the same families, and also quotes the genealogic trees of Hurst,<sup>5</sup> Pel,<sup>6</sup> Dickinson,<sup>7</sup> and Kidd,<sup>8</sup> in which heredity and familial arterial disease and nephritis are traced back through three generations of each family.

The rôle of heredity is equally important in relation to arterial disease. This has been most happily expressed by Osler,<sup>9</sup>

who said, "The onset of what might be called physiologic arteriosclerosis depends, in the first place, upon the quality of the arterial tissue, 'vital rubber,' which the individual has inherited, and second, upon the amount of wear and tear to which he has subjected it."

The case here reported is believed to exemplify hereditary and familial arterial disease. It is true that this patient was first observed at the stage of his illness where the clinical diagnosis was chronic glomerulonephritis. Some members of his family have arterial disease, others have died of vascular catastrophes. Either nephritis alone, arterial disease alone, or both combined, as in this patient, would serve equally well as a text.

#### CASE REPORT

G. K., male, aged forty, married. Was admitted to the medical service of this hospital on March 27, 1924 with the following history:

**Chief Complaints.**—Weakness, pallor, loss of weight.

**History of Present Illness.**—For the past five years patient has been under treatment for high blood-pressure, first observed incident to an examination for insurance. Two years ago studies of the blood and spinal fluid revealed negative Wassermann reactions. He appeared to be in reasonably good health until three months ago, when he began to complain of undue fatigue, loss of weight, and severe headaches, but was able to continue uninterruptedly with his work until five weeks ago, when more severe headache, greater weakness, and marked disturbance of vision were noted. Five weeks ago, without medical advice, he placed himself under the care of a physiotherapist, who treated him by drastic elimination, frequent cabinet sweat baths, and brisk saline purgation. Since the beginning of this treatment he has rapidly grown weaker and has been confined to bed for the past two weeks.

**Previous Medical History.**—Had scarlet fever in early childhood, carbuncle on back four years ago, no glycosuria. States specifically that he has never had rheumatic fever, chorea, or tonsillitis.



**Social History.**—Salesman by occupation; alcohol and tobacco in moderation; denies venereal infection.

**Family History.**—Sister, H. K., died at the age of forty-three. One year prior to her death, at the age of forty-two, she was suddenly stricken with a right-sided hemiplegia, with resultant paralysis of the right arm and right leg.

Sister, Mrs. C. C., aged forty-five, is at present under the care of Dr. C. B. Weinberg, of Atlantic City, who extended to me the courtesy of examining his patient. She has had hypertension for the past two years. Examination on April 10, 1924 revealed a systolic blood-pressure of 210.

Sister, Mrs. M. C., aged thirty-two, is under the care of Dr. I. Jesse Levy, of New York. She has been married for twelve years and has 2 children who are living and well. She has had two miscarriages. She has never had scarlet fever. Following acute follicular tonsillitis at the age of fourteen she developed acute nephritis. There were no renal complications during pregnancy. Several years ago she was advised by her family physician that she had high blood-pressure and "kidney trouble." Numerous Wassermann tests have been made. Examination in April, 1924 revealed a systolic blood-pressure of 180.

Brother, L. K., aged thirty, married, was examined in April, 1924. He appeared to be at least ten years older than his stated age. Systolic blood-pressure 146.

There were 7 children in this family. The 2 not enumerated died at the ages of six months and three years respectively of unascertainable causes.

The father of these children died at the age of fifty of pneumonia, having had diabetes for eleven years prior to his death. He had 6 brothers, all of whom are dead and all of whom are said to have had diabetes. This fact was stated independently by each member of the family examined, but due in part to the fact that 5 of these deaths occurred in Europe it cannot be substantiated.

The mother died at the age of sixty-three of apoplexy. She was the oldest of 13 children. Eight died at birth or in infancy. One died at the age of twelve, one at twenty-eight. Causes of

death unknown. One died at the age of fifty-three, she is said to have had locomotor ataxia. One is still living, whose whereabouts is unknown.

**Physical Examination.**—Patient is apparently gravely ill. He is apprehensive, restless, and irrational. He presents the picture of severe anemia. The peripheral vessels are moderately sclerosed. The heart is enlarged to the left; there is marked accentuation of the second aortic sound. Nothing abnormal noted in the lungs or abdomen. The reflexes are exaggerated.

**Clinical Examination.**—Blood-pressure, systolic 205, diastolic 125. Urine, specific gravity 1009; albumin, trace; sugar, negative. On microscopic examination numerous hyaline and pale granular casts, a few waxy casts. Blood count, hemoglobin 46 per cent., red blood-cells 2,740,000. Blood plasma carbon dioxide, 48 volumes per cent. Blood Wassermann negative. Phenolsulphonephthalein test, no elimination in two hours. Blood urea nitrogen, 102 mg. per 100 c.c.

Eye examination (Dr. B. F. Baer, Jr.): "General retinal edema, veins full, arteries reduced and extremely tortuous. Eye-grounds bespattered with hemorrhages and areas of degeneration."

The patient rapidly became uremic, the blood urea nitrogen reaching 204 mg. four days prior to death. The urinary output at no time was greatly reduced below the fluid intake. On April 3, 1924 patient had numerous convulsions and became stuporous. Bronchial pneumonia developed and death ensued, in uremic coma, on April 7, 1924.

Dr. Baldwin Lucke performed the autopsy and I am indebted to him for the following report:

**"External Inspection.**—White male, forty years old; weighing about 75 k.; measuring 170 cm.; well built; well nourished; rigor and livor well established. Skull is normal in size and shape. Eyes, ears, and nose are negative. Practically all of the teeth are present; a few show signs of decay. Thorax and abdomen are negative. External genitalia and extremities show nothing of note. There is no edema or glandular swelling.

**"Internal Inspection.**—Panniculus averages 2 cm.; is nor-

mally fleshy. Muscles are dark red and fleshy throughout. Peritoneum is smooth and glistening; contains a few cubic centimeters of clear serum. Viscera occupy normal position. Right diaphragm extends to the fourth rib; left, to the fifth rib. Thoracic walls are normal. Right lung is free from adhesion and the left pleural sac is obliterated. There is no free pleural fluid. The pericardium contains a few cubic centimeters of clear serum.

**"Detailed Inspection.**—*Aorta.*—Has normal caliber and a slightly diminished elasticity. There are numerous slightly elevated, hyaline, and very atheromatous patches throughout the entire vessel, but calcification is not evident.

*"Heart.*—Weighs 500 gm.; moderately enlarged and normal shape. Epicardium is moderately fatty. The coronary vessels are conspicuous, stiffened, and slightly tortuous. Muscle is firm, reddish brown, and fleshy throughout. Left ventricular wall measures 22 mm.; right, 3 mm. Papillary muscles and chordae tendineae are normal. Valve leaflets are delicate and have normal shape. The bases of the mitral show a few small atheromatous patches. Foramen ovale is closed. The coronaries have an irregular intima, with many atheromatous and hyaline elevations.

*"Left Lung.*—Weight 850 gm.; the posterior half of the basal lobe is firm, purplish red, and the pleural surface is covered with a fine film of fibrin. Section through it shows dull, reddish-brown, finely granular consolidation which involves the major portion of the posterior half. The consolidation is not uniform, but has a patchy confluent character. The rest of the lung tissue contains a moderate excess of frothy, blood-stained fluid. The bronchi have a slightly reddish mucosa and a normal diameter.

*"Right Lung.*—Weighs 700 gm.; resembles its fellow, except that the patchy consolidations of the basal lobe are less conspicuous.

*"Spleen.*—Weighs 220 gm.; moderately enlarged, firm. Capsule is smooth and translucent. Cut surface is dark red. Trabeculae conspicuous. Follicles indistinct. Pulp has a reddish-brown tint.

"*Adrenals.*—Are normal in size and soft. Cortical zones are yellowish. Medullæ is grayish red.

"*Right Kidney.*—Weighs 150 gm.; measures  $11 \times 5\frac{1}{2} \times 3\frac{1}{2}$  cm.; moderately flaccid. Capsule flaccid and adheres slightly to a mottled, deep red, and reddish-brown surface which is be-



Fig. 149.—Section of kidney. The capsular epithelium is proliferated, forming a typical "demilune." The tuft in the center is atrophic. The tubules are either dilated (upper part of photo), contain red blood-cells (right part), or are collapsed and atrophic (lower part of photo).

ginning to show an even, fine granularity. Cut surface is bloody. Cortex and medulla are poorly differentiated; the former averages 5 mm.; its striations are indefinite. Glomeruli are difficult to see, but can be made out. Vessels at the corticomedullary junction are slightly stiffened. Medullary striations are dusky.



Fig. 148.—Water color sketch of kidney made immediately postmortem ( $\frac{2}{3}$  actual size). The gross pathology is described in the autopsy protocol.



Peripelvic fat is normal, not thickened. Pelvic mucosa is thin and smooth.

"*Left Kidney*.—Weighs 145 gm.; resembles fellow.

"*Urinary Bladder*.—Contains about 100 c.c. of slightly turbid fluid. Mucosa is pale, unbroken, shows no traces of inflammation.

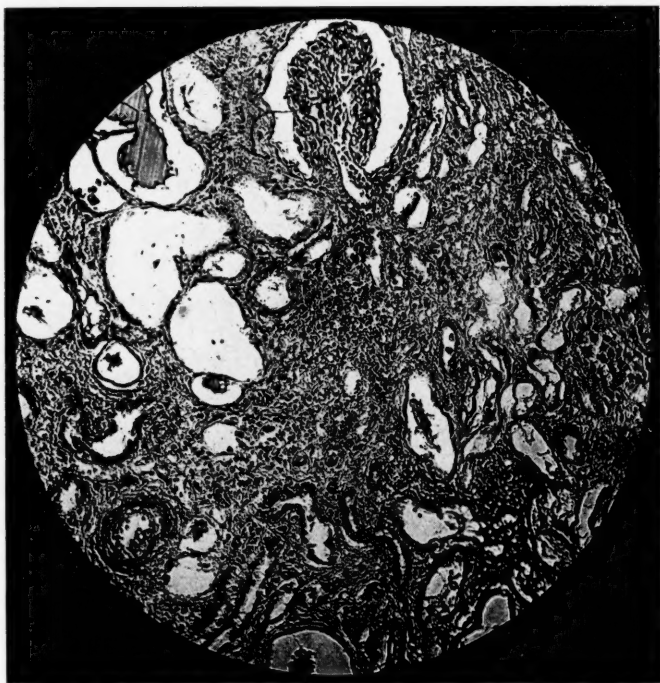


Fig. 150.—Section of kidney. High power photograph to show dilatation of tubules and overgrowth of stroma.

"*Prostate and seminal vesicles* are normal.

"*Esophagus* is normal.

"*Stomach* is normal in size. Walls are of normal thickness. Mucosa is pale, velvety, covered with a small quantity of thin mucus. Sphincters are normal.

"*Liver*.—Weighs 1900 gm.; moderately enlarged; pale brown, somewhat doughy. Surface smooth. Capsules thin. Cut surface pale brown, has a fatty sheen. Lobulations are very distinct; centers have preserved normal color; peripheries are pale yellowish brown.

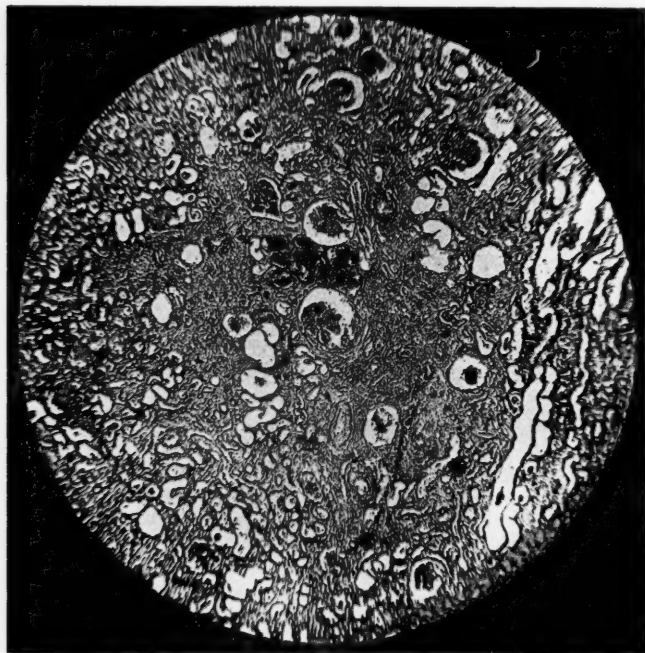


Fig. 151.—Section of kidney. Low power photograph to show general increase of stroma, dilation or collapse of tubules, and proliferation of capsular epithelium. Some of the glomerular tufts are atrophic, others are richly cellular.

"*Gall-bladder*.—Contains a stone  $5 \times 2\frac{1}{2} \times 2\frac{1}{2}$  cm.; is moderately firm, has a smooth yellowish surface. The mucosa of gall-bladder is thin.

"*Pancreas and intestines* are normal.

"**Gross Anatomic Diagnosis.**—*Aorta*.—Arteriosclerosis.



*"Heart.*—Hypertrophy; coronary arteriosclerosis.

*"Lungs.*—Bilateral confluent lobular pneumonia.

*"Spleen.*—Fibrosis.

*"Kidneys.*—Chronic glomerulonephritis.

*"Liver.*—Fatty infiltration.

*"Gall-bladder.*—Cholelithiasis."

Dr. Allen J. Smith, Professor of Pathology, kindly examined the kidneys and the microscopic sections, and his conclusions may be briefly summarized: "There is no doubt that this case can be classified as true chronic glomerulonephritis as evidenced by the changes in the glomeruli, but in a comparatively early stage, as many of them still preserve their normal appearance. This would not be the case were the underlying process one of infection such as is seen in scarlet fever, where there would be more generalized glomerular changes. The fault does not seem to be primarily within the arteries themselves. Were such the case practically all the glomeruli in any given area would be atrophied and replaced by scar tissue, due to gross interference with their blood-supply. In addition to this the arterial changes in these sections are not in the intima. The changes present in the capillaries are due to an overgrowth of fibrous tissue in the adventitia. The underlying fault seems to be in the growth of connective tissue *around* the blood-vessels, mechanically interfering with their blood-supply. Suspect that the process here is identical with that which in its early stage is recognized clinically as benign hypertension. As the perivascular fibrosis continues secondary changes in the glomeruli are produced, and the kidneys begin to contract and diminish in size. From a pathologic viewpoint there is sufficient change in the liver, both cloudy swelling of the hepatic cells and replacement of liver cells by fatty infiltration, to be a factor in the production of uremia."

It is interesting to think of the relation of heredity to human ills in a broader sense than that which is illustrated by this case report. This relationship, perhaps, is appreciated in a general way, but is not always thought of in its application to an in-

dividual case. Many years ago this thought was well expressed by Francis Galton,<sup>10</sup> who said, "The world is beginning to perceive that the life of each individual is in some sense a prolongation of his ancestors. The life history of our relatives are especially able to forewarn and encourage us, for they are prophetic of our own futures."

Numerous writers, Babes,<sup>11</sup> Coplin,<sup>12</sup> Weiss,<sup>13</sup> and others, have reported series of cases of renal hypoplasia due to defective arteriogenesis. In all of these the kidneys are very small and usually unequal, one being markedly hypogenetic. The contention of Coplin is that these hypogenetic kidneys were never perfectly developed, that the arteries were always defective, and that probably the renal hypoplasia rested on a nutritive basis. Although the family history of this patient was indicative of this condition, the findings postmortem indicated that such was not the case.

**Summary.**—There is presented a case of glomerulonephritis in a man forty years of age, with marked hypertension for at least five years prior to his death.

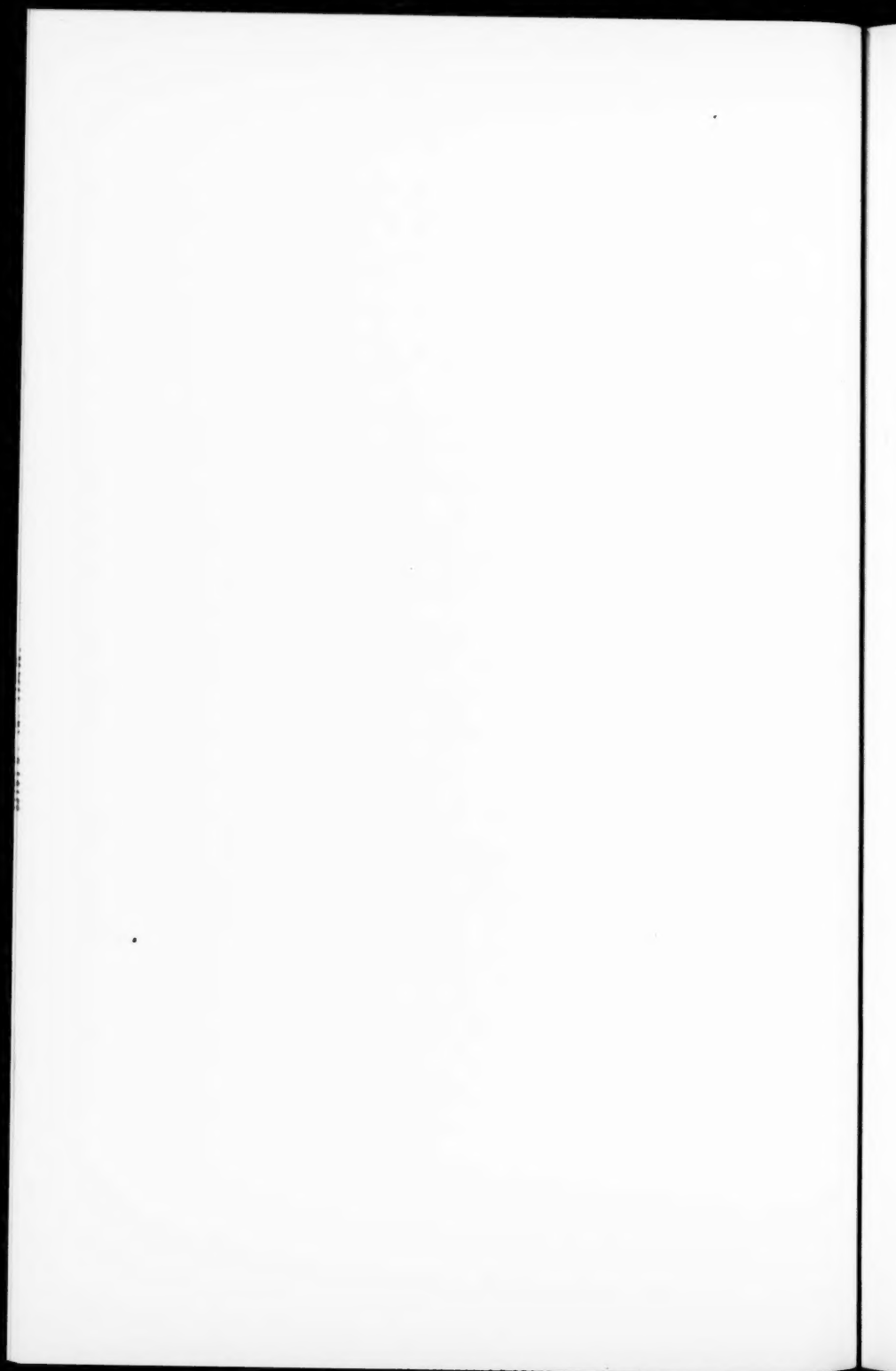
The family history of arterial and renal disease is emphasized. It is believed that the most important etiologic factor in this case is, to quote Oliver Wendell Holmes, "the inability to pick one's ancestors."

The autopsy findings indicate that in this particular patient, although the final disease was glomerulonephritis, yet it probably began with what we understand clinically as benign hypertension. This conception helps to explain the fact that in this and in similar families studied, vascular changes occur in some, and renal changes predominate in others in the same family. Perhaps the perivascular involvement is the fundamental pathologic process, the clinical manifestations expressing the stage to which it has progressed.

In this case both kidneys were approximately of equal size and normal weight; therefore it should not be included in the group of congenital renal hypoplasias. It is not an example of hypogenetic nephritis.

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## CLINIC OF DR. LEON JONAS

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### HYPOGLYCEMIA

HYPOGLYCEMIA has become an important clinical entity since the discovery of insulin because overdosing with this therapeutic agent may cause weakness, sweating, nervousness, convulsions, stupor, and death.

Before the discovery of insulin clinical hypoglycemia was comparatively unknown. There are several reasons for this. In the first place the symptoms are mild and not recognized as due to low blood-sugar. Second, this recognition was made possible by the discovery of microchemical methods enabling one to determine blood-sugar concentration. Furthermore, it will be found on examining the published blood-sugar values that there is no unanimity of opinion as to the normal minimum concentration, the lowest being reported as 0.044 per cent. From the more recent figures one might accept the normal fasting range of blood-sugar to be from 0.08 to 0.12 per cent. The symptoms of hypoglycemia usually begin to appear when the blood-sugar is 0.07 per cent., the lower the concentration, the more alarming the symptoms become.

It is known that, after a carbohydrate meal, there occurs an increased concentration of the blood-sugar followed by a fall. Folín and Berglund<sup>1</sup> believe that the fall of this concentration below the fasting level to be normal and regular.

I shall review briefly the work on experimental hypoglycemia so that a clearer understanding of the possible mechanism involved in clinical hypoglycemia may be had. Most experimental work has to do with the liver and the adrenals.

Bock and Hoffman<sup>2</sup> as early as 1874 showed that after ligating the vessels of the liver the blood-sugar disappeared in three-quarters of an hour. These results, at least the production of a marked hypoglycemia, have been confirmed by others after the removal of part of the liver or ligations of its vessels.

More recently Mann and his co-workers<sup>3</sup> studied the effects of the removal of the liver in dogs and other animals. They found after the removal of the liver from dogs that during the first few hours the dogs acted like other animals that had undergone different operative procedures. They also found that the blood-sugar concentration began to drop. After three to five hours the animals would develop muscular weakness, loss of reflexes, muscular twitchings, convulsions, coma, and finally die. The drop in the blood-sugar concentration bore a definite relation to the development of the above symptoms. At the time of death there was barely a measurable amount of sugar in the blood. Death usually occurred one to two hours after the development of the first symptoms. If, however, glucose was administered to these animals after stupor developed they recovered almost immediately from the stupor and were able to walk around.

It has been found that such chemicals as hydrazin, chloroform, and phosphorus, which have a selective toxic effect on the liver, cause a hypoglycemia and a marked decrease in the glycogen content of the liver.

Underhill<sup>4</sup> in his study of the effect of hydrazin on carbohydrate metabolism noted the marked hypoglycemia and the complete or nearly complete disappearance of glycogen from the liver. This occurred in spite of the injection of large quantities of carbohydrates. He stated that the symptoms of extreme weakness that developed in the dogs after hydrazin may be directly correlated with the diminished store of carbohydrate as indicated by the lowered blood-sugar concentration. The above experiments emphasize the important part played by the liver in carbohydrate metabolism.

The relation of the adrenals to carbohydrate metabolism has been the subject of much study. Porges<sup>5</sup> and many after him

claimed from their experimental work that the removal of these glands caused hypoglycemia. Their results are now questioned. Stewart<sup>6</sup> did not find the glycogen function of adrenalectomized rabbits and rats to be essentially altered. Stewart criticizes the conclusions of Porges and those who found similar results because their observations were made on dying animals which had undergone a severe operation and had not been eating. A French observer found recently that rabbits were more sensitive to insulin after adrenalectomy than before the removal of the adrenals.

Cannon, McIver, and Bliss,<sup>7</sup> experimenting on cats with denervated hearts, have revealed a mechanism or series of mechanisms having the function of maintaining the physiologic percentage of blood-sugar when there is a danger of deficiency. They state that if the blood-sugar falls below a critical point in consequence of a deficiency, splanchnic neurones of the sympathetic system are set in action as indicated by increased adrenal secretion. Both the nerve impulses and the increased secretion of adrenin have the effect of liberating sugar from the liver into the circulation, thus tending to restore the disturbed equilibrium. This they regard as the first line of defense against the falling blood-sugar concentration. If the first defense fails to prevent the blood-sugar from falling there is a second stage in which the activities of the first stage are intensified. This stage is also associated with increased adrenal secretion and may culminate in convulsion.

The influence of the thyroid and other endocrine glands on carbohydrate metabolism has been investigated by many, with conflicting results. Janney and Isaacson<sup>8</sup> found a decrease in the fasting level of dogs after thyroidectomy, the lowest concentration in their 5 dogs was 0.063 per cent., a very mild hypoglycemia.

#### CLINICAL HYPOGLYCEMIA

Insulin hypoglycemia is so familiar to most clinicians that it will not be discussed here. I shall endeavor to direct your attention to other clinical conditions where hypoglycemia has been found.

There are many cases reported with low blood-sugar concentrations, but many of these are dubious because, as stated before, it has been only in the last few years that accurate methods for the determination of blood-sugar have been available. Hypoglycemia has been found chiefly in connection with conditions where there were weakness and asthenia.

Allen<sup>9</sup> has pointed out that the normal blood-sugar concentration is maintained throughout long fasts. Jansen<sup>10</sup> however, found in a study of the blood-sugar in 24 patients suffering from edema of undernutrition, 12 who had blood-sugar concentrations from 0.034 to 0.07 per cent., the other 12 being normal. He accepts 0.08 to 0.10 per cent. as the normal fasting range.

There are numerous instances, especially conditions involving endocrine glands, where there is a mild hypoglycemia. In this group are included, particularly, cases of myxedema, cretinism, and hypopituitarism. Hypoglycemia has been found in cases of Addison's disease. It may be of particular significance in this condition because of the marked weakness found in this disease.

McCrudden and Sargent<sup>11</sup> found the fasting blood-sugar concentration in a case of progressive muscular dystrophy to be 0.064 per cent. Their observation is particularly important because they believed the hypoglycemia to be the cause of the weakness in their case. They found that when they gave the patient sufficient carbohydrate to raise the blood-sugar concentration they brought about an increase in health, strength, and weight of the patient.

Recently Levine, Gordan, and Derick<sup>12</sup> examined the blood of 11 marathon runners before and immediately after the race. Those who had a marked hypoglycemia presented a picture of shock similar to that produced by an overdose of insulin, such as muscular twitching, pallor, moist skin, irritability, collapse, and stupor. Those with a normal blood-sugar showed no symptoms of shock.

Holman<sup>13</sup> reported the case of a girl seventeen years old who twenty-four hours after a subtotal thyroidectomy for ex-



ophthalmic goiter, became very restless, weak, and finally stuporous. The blood-sugar at this time was 0.048 per cent. The intravenous injection of 200 c.c. of a 20 per cent. glucose solution caused prompt recovery from the above symptoms. She relapsed into this state six hours later and was again relieved by the injection of glucose. She finally fully recovered from the operation. He has seen 2 other cases with low blood-sugar concentrations after thyroid operations.

Hyperglycemia due to deficient pancreatic hormone has been recognized for many years, but the opposite condition, where there is an overproduction of the pancreatic hormone or whatever mechanism is involved, has been suggested only recently.

Harris<sup>14</sup> has reported 3 cases of hypoglycemia in patients not treated with insulin. The symptoms in 2 non-diabetic patients were weakness, nervousness, and hunger one hour before meals. They were relieved for three or four hours after taking food. The blood-sugar in both cases at the height of the symptoms was between 0.06 and 0.07 per cent. When these patients took food every three to five hours they remained free of symptoms. His third case was a woman who had had transient glycosuria twice in the previous eighteen months. Her symptoms were weakness, nervousness, and hunger, which were relieved by taking an orange. Her blood-sugar concentration during one of these attacks was 0.047 per cent.

Hartman and Reimann reported an unusual case of hypoglycemia before the Physiological Society of Philadelphia at a recent meeting. Their patient, a man, suffered from hunger, and marked weakness three to four hours after meals. On several occasions he became unconscious. The blood-sugar during these attacks was below normal. Frequent feeding during the twenty-four hours relieved him of symptoms and permitted him to enjoy good health.

The occurrence of spontaneous hypoglycemia, in a diabetic a number of days after insulin therapy was discontinued, is illustrated by the following cases:

W. W., colored, male, age fifty years, was admitted to the medical ward of the University Hospital March 17, 1923, because of diabetic gangrene of the toes of both feet. His history is as follows: Three years before admission he began to have polyuria and thirst. His urine at that time contained glucose. He was placed on a diet, but followed it indifferently. December 24, 1922 a chiropodist removed corns from the toes of both feet. The site of the corns became infected and did not heal in spite of medical attention.

The patient was a sturdy, well-developed negro. The examination of head, neck, and trunk was negative. There were no tremors, palsies, nor atrophies. Sensation for touch, pain, and temperature was preserved. The radial arteries were just palpable. The biceps and triceps reflexes were normal. The patellar reflex was feeble. Pulsation was not felt in the dorsalis pedis artery of either foot. The skin of the toes of both feet was black. The gangrene was of the dry type. He had a mild septic fever.

Blood-pressure was 150 systolic and 80 diastolic. The Wassermann reaction was negative. The urine on admission contained sugar, but no acetone nor diacetic acid. The fasting blood-sugar on the morning following admission was 0.168 per cent. The plasma  $\text{CO}_2$  content was forty-five volumes per cent.

**Treatment.**—On admission he was placed on a diet containing 70 gm. of protein, 60 gm. of fat, and 20 gm. of carbohydrate. He became sugar free in a few days and the diet was increased gradually to 70 gm. protein, 130 gm. fat, and 80 gm. carbohydrate. On this diet the urine remained sugar free until April 16th, when it began to show traces of sugar, but no ketones. During this period the condition of his feet became worse necessitating amputation of both feet  $1\frac{1}{2}$  inches behind the metatarsophalangeal articulation. In spite of the operation his condition continued to grow worse, there being continued fever and loss of weight. The stumps became infected. During this period his tolerance for carbohydrate slowly decreased, but at no time did ketones appear in the urine. On May 28th both

legs were amputated at the upper third of the thigh. Sloughing occurred at the sites of the operation.

Because of the gradual loss of tolerance insulin therapy was begun May 1, 1923. He was given 60 gm. protein, 80 gm. fat, 60 gm. carbohydrate, and 5 units of insulin before each meal. On this régime his urine remained free of sugar and ketones except for an occasional trace of sugar. On May 9th insulin was reduced to 5 units twice a day, the diet at this time being 60 gm. protein, 140 gm. fat, 60 gm. carbohydrate. On June 3d the patient refused to eat after receiving insulin and symptoms of insulin shock developed.

His fasting blood-sugar the following morning was 0.063 per cent. Insulin therapy was discontinued after June 3d. He was continued on a diet of 60 gm. protein, 100 gm. fat, 60 gm. carbohydrate. The urine remained sugar free. During this period he gradually became weaker, although he ate all his food and had no diarrhea. On June 14th, eleven days after insulin had been discontinued, he suddenly became delirious and then comatose. His blood-sugar at this time was less than 0.030 per cent. Glucose was given intravenously and he became conscious almost immediately. During the remainder of the day his carbohydrate intake was greatly increased. He continued to be rational until 10 P. M., when he again became comatose. This time he did not respond to glucose given intravenously, and died a short time afterward.

The important feature of this case was the development of a spontaneous hypoglycemia ten days after insulin therapy had been discontinued. The explanation of this hypoglycemia is unsolved. The probability of it being due to delayed insulin effect is possible, but this explanation can only be proved or disproved after our experience with insulin has extended over a longer period. It is known that glyckinin, the insulin extracted from vegetables, exhibits a delayed effect when given to animals. Unexplained spontaneous hypoglycemia is known to have occurred in cases of diabetes on restricted diets without insulin. Our case may fall into this group.

The recognition of a state of hypoglycemia in the variety of

conditions mentioned above brings to our attention the relative frequency with which it occurs in clinical medicine. In all instances the patients suffered in varying degrees from those symptoms which occur after overdosage with insulin, such as weakness, sweating, rapid pulse, and nervous phenomena.

The importance of recognizing this condition must be emphasized because, first, if due to hypoglycemia relief can be obtained usually by administering carbohydrate; second, occurrence of the symptoms can be avoided by giving sufficient carbohydrate to keep the blood-sugar concentration above that level at which the symptoms of hypoglycemia develop.

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## CLINIC OF DR. EDWARD WEISS

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### A CONSIDERATION OF CERTAIN FORMS OF NEPHRITIS. NOTES ON ETIOLOGY, FUNCTION, AND TREATMENT

GENTLEMEN: In bringing the following cases before you it is not my purpose to attempt an orderly presentation of the subject of nephritis, but rather to emphasize some of the points that arise in discussion. The first one will permit us to discuss the etiology of an unusual renal lesion, the second will demonstrate the prognostic value of certain functional tests, and the last two will give us an opportunity to consider the dietetic management of some of the forms of nephritis that have edema as an outstanding feature.

The first case that I present to you is not a common one, but occurs often enough to be of intimate concern to all of us. The patient is a normal enough looking boy now, but he has recently had a narrow escape from death, and it is chiefly for that reason that I bring him before you.

**Case I.**—J. D., a white boy aged thirteen, was admitted to the Jefferson Hospital<sup>1</sup> on February 15, 1924, with convulsions. On February 12, 1924, three days before admission, his tonsils had been removed. Headache developed the following day, and on the 14th became much more severe. That afternoon, about 3 o'clock, he had his first convulsion, and after this he was unable to see. He had two more convulsions before admission to the hospital.

<sup>1</sup> This case and the ones that follow are from the medical service of Dr. S. Solis Cohen, to whom I am greatly indebted for the privilege of studying and reporting them.

The past history was of some importance. He had measles in childhood, but never had scarlet fever or diphtheria. He was a chronic bed-wetter, wetting the bed nearly every night. The family history was negative for kidney disease, hypertension, or heart disease.

On admission the boy was delirious and was having frequent convulsions; his skin was hot and dry and his face flushed. Dr. Herff, the resident physician, at once instituted treatment. The boy was sweated, and later his stomach and bowels were thoroughly irrigated; this was followed by purgation. He responded very promptly to treatment, and by the next day was pretty well out of danger. It may be truly said that his skin saved his life. For the next few days he was carefully studied, and the diagnosis of nephritis established. His urine contained a heavy cloud of albumin, no pus or blood-cells, but a considerable number of hyaline and granular casts.

After he was in comparatively good shape his blood-pressure was 130/72; his phenolsulphonephthalein excretion in two hours was 25 per cent.; his blood-urea nitrogen 20 mg.; blood Wassermann negative. The eye-grounds showed slight blurring of the margins of the disk, but no other changes. The heart seemed somewhat enlarged, but there was no thrill or murmur; the peripheral vessels seemed slightly harder than normal.

Sweating was continued daily for a week, then every other day for two weeks, and then discontinued. During the first few days he was given liquids freely; later no particular attention was paid to his diet. He was discharged from the hospital on April 19th in good condition, with instructions to report to the Out-patient Department.

The diagnosis was chronic renal disease, with an exacerbation (fulminating uremia) following tonsillectomy.

The first point demanding our attention is the etiology of this renal lesion in a boy of thirteen, who had always enjoyed good health. He had never had a serious illness, nor any of the ailments that are sometimes followed by renal disease, such as tonsillitis, scarlet fever, and diphtheria. The tonsillectomy had been advised because his tonsils were of the large, cryptic, and

obstructive variety. The fact that he was a chronic bed-wetter assumed more importance when we learned by comparing his day and night urine output that his night amount was definitely increased. I feel, therefore, that we may assume that it had been so for many years and, together with the enlarged heart and slightly thickened peripheral vessels and eye-ground changes, is a point in favor of a suggestion I am about to make. That is, that this boy suffers from a congenital renal lesion; that he was born with kidneys below par, capable of meeting the ordinary demands on renal function, but incapable of responding to such a strain as etherization and tonsillectomy. Such cases I have before observed,<sup>1</sup> and from necropsy study it was my feeling that the kidneys presented an unusual appearance; that they seemed naturally small (hypogenetic) rather than shrunken. This picture, together with microscopic evidence of degeneration and extensive fibrosis, and no history of renal disease or illnesses commonly followed by renal disease, persuaded me that just as we may be born with "poor rubber" in our arteries, so we may be born with kidneys not quite capable of meeting unusual demands, susceptible to infection, and certain to break down prematurely. This is a hypothesis difficult to prove, but I feel convinced that there is a form of chronic nephritis of congenital origin which sometimes occurs in several members of a family, and often has an hereditary basis.

The next point to engross our attention is the fact that this nearly fatal accident might have been avoided by more attention to urinalysis before operation. I have learned that his urine was studied the morning of the operation, but that the result, showing albumin and casts, was delayed in reaching the surgeon, who operated thinking the examination negative. This near-tragic accident should impress us all as to the necessity for thorough study of the urine before the administration of an anesthetic.

Another point which will interest you is that here was uremia with convulsions without nitrogen retention. In a large number of determinations this boy's blood-urea nitrogen was never more than 24.

Prognosis is a matter of grave concern to us. What are this lad's chances for recovery from his present trouble—and what will be his expectation of life? Do not be misled by his

TABLE I.  
A comparison of the findings in Case I.

		February	April	June
Height		74½	90	95
Blood Pressure		130/72	120/70	170/80
Hemo-globin		67%	68%	85%
Eye Grounds		Slight blurring of margins of discs, both eyes	low grade optic neuritis	low grade optic neuritis of right eye
Heart and Vessels		Slight enlargement; a little thickening	Same	Same
Edema		None	None	None
Urine	24-hr. out-put	1500 cc.	Same	1750 cc.
	anal-ysis	Heavy cloud albumin, occas. pus cell, no red blood cells, few myelin and granular casts	Light cloud of albumin; no pus cells, no red blood cells, occas. myelin and granular casts	Same
Phthalein.		25%	25%	58%
Blood urea nitrogen		20	Varied from 16 to 24 during March and April	17
Day to night ratio		1000 to 600 cc. (not exact)	1000 to 750 cc.	850 to 900 cc. 2-hr. test— sp. gr. variation 1020 - 1030 Large night urine sp. gr. 1025
Diet		No particular attention	Same	General restriction

prompt response to treatment in the early days of his illness, nor by his good behavior in the weeks that followed in the hospital. To show you the necessity for caution I present his



later record, with a review of his findings five months after his accident (Table I).

During the months that followed his attack of uremia this boy took on 20 pounds in weight, his blood-pressure rose from 130 to 170 systolic, and he suffered from occasional headaches. Otherwise he seemed in perfect health. Nevertheless his urine still showed a cloud of albumin, hyaline and granular casts, and the eye-ground study revealed a low-grade optic neuritis in the right eye. A two-hour specific gravity test showed fixation at a high level and a large output of night urine. The urea nitrogen was 17, and, curiously enough, the phenolsulphonephthalein excretion had increased from 25 to 58 per cent. (several tests), showing that one must not rely upon only one method for judging renal function in evaluating a case.

He was now put upon a well-balanced diet just sufficient to meet his caloric needs—overeating, by giving the kidneys extra work, probably had much to do with the rise in blood-pressure. In a short time his blood-pressure came down to 110/60, and he was again discharged from the hospital to recuperate in the country.

I need hardly tell you that this boy leads a precarious existence; that any great strain, such as an infection, is apt to break down his small renal reserve and again induce uremia. Even though he be carefully guarded against infection, overeating, and overwork his life expectancy is far less than normal, for his kidneys are a weak link in the cardiovascular renal chain, and we may expect to hear from him some day with the symptoms and signs of advanced chronic renal disease.

The second case has an even less hopeful outlook, and demonstrates the prognostic value of certain functional studies.

**Case II.**—N. V. F., a white man aged thirty-eight, who was admitted to the Jefferson Hospital on February 24, 1924, complained of nausea and edema of the legs. His family history was unimportant. He had measles, mumps, and scarlatina in childhood, from all of which he had made an uneventful recovery. In 1904 he had a mild attack of typhoid fever.

His present trouble began suddenly, in June, 1923, at which time he had an infection beginning with sore throat (which he states was influenza), and which kept him in bed for five days. During this time he passed small amounts of "coffee-colored" urine. Early in July his feet became swollen, and he found that he had to get up two or three times during the night to urinate. Later he became nauseated and lost weight and strength.

On admission to the hospital he was pale and edematous and looked very ill. His breath was heavy; tongue coated; teeth bad; gums infected; his tonsils were small and embedded, and chronically diseased. His heart was somewhat enlarged; there was no murmur or thrill, but the sounds were of poor quality. The abdomen contained some fluid, the abdominal walls were edematous, and the legs and scrotum were markedly swollen. The blood-pressure was 170/90 and his weight was 169 pounds. The urine was acid in reaction, contained a heavy cloud of albumin, pus and blood-cells, and was loaded with hyaline and granular casts. This, with the history, was sufficient to confirm the diagnosis of acute nephritis. The blood-count was hemoglobin 53 per cent., red cells 2,700,000, white cells 16,850. His phenolsulphonaphthalein excretion was 25 per cent. in two hours; blood-urea nitrogen 18 mg., plasma chlorid 330 mg., the two-hour specific gravity test showed fixation at a fairly low level, and a large output of night urine.

The electrocardiogram revealed ventricular premature contractions and evidences of myocardial degeneration.

Upon a bland, low protein diet, with restriction of fluids, and with sweats and purgation, he became free of edema about March 1st, and seemed considerably improved. His blood-pressure dropped to 130/70, but his blood-urea nitrogen, in spite of the apparent clinical improvement, had gradually risen from 18 to 35. Nevertheless we felt it best to remove his infected tonsils, and this was done under local anesthesia, without difficulty. He did very well after the operation, and was discharged on March 22d, with a note that "he seems markedly improved, is free of edema, feels well, and says his strength is returning."

He did not live in Philadelphia, and we did not see him again

until May, about six weeks after discharge. In Table II his findings are compared with those of his previous admission, and you will note that although he has gained in weight (no edema) and feels comparatively well, his urine still shows al-

TABLE II  
A comparison of the findings in Case II.

		March	May
Weight		132	138 1/4
Blood pressure		130/70 -- 140/80	150/80 -- 170/90
Urine	24 hr. output	1600 -- 1800 cc.	1600 cc.
	Analysis	Heavy cloud albumin, many pus cells, occasional trace of blood, many hyaline and granular casts.	Same
Hemoglobin		56%	50
Phthalein		25%	No excretion (2 tests)
Blood urea-Nitrogen		35 Mg.	60 Mg.
Plasma chlorides		330 Mg.	684 Mg.
2 hr. sp. gr. test		Tendency to fixation at low level, 1012 - 1016; night urine 550 cc. specific gravity 1015	Fixation at higher level, 1015 - 1020; night urine 840 cc. sp. gr. 1015

bumin, pus, blood, and casts; the blood-pressure has risen, he has no excretion of phenolsulphonephthalein, the blood-urea nitrogen has almost doubled, and the two-hour specific-gravity test shows even graver derangement of function than before. The electrocardiogram now shows left ventricular preponderance,

indicating cardiac hypertrophy as a complication of his renal disease.

In this case we note the value of laboratory studies in nephritis. Without such studies we might have been led astray by his apparent improvement. As a result of them we know that he is doomed. We are dealing with a rapidly progressive acute renal lesion, due to a probable streptococcic infection, and in spite of our efforts to ease the burden on the diseased kidneys by the removal of the infected tonsils, by rest, purgation, sweating, and dietary precautions, we cannot stay the progress of this malignant lesion.

One more point before dismissing this case. Why do we term this lesion acute when we know that it is very rare to find a first attack of nephritis coming on at the age of thirty-eight, and that more often it is but an exacerbation of a chronic renal lesion? It is possible that this man has had previous trouble, such as at the time of his scarlet fever in childhood; but careful questioning fails to bring out any single hint in his past history to suggest kidney disease, and we are therefore led to conclude that all of his present trouble is due to his infection in June.

I am glad now to present to you a young woman with a mild renal lesion, who has a much happier outlook than the 2 previous patients.

**Case III.**—F. K., a Jewess, aged nineteen, was admitted to the Jefferson Hospital on February 11, 1924. Her only complaint was edema of the eyelids and feet. Her family history was unimportant. She had measles and mumps in childhood, but never had scarlet fever, diphtheria, rheumatic fever, or tonsillitis.

She had two attacks of influenza in 1918, but made a good recovery from both.

On the night of January 24, 1924 the patient went riding in an open car and "was chilled." The following morning her feet were swollen and her physician found albumin and casts in her urine.

On admission to the hospital we found a pale, but fairly well-

nourished girl. Physical examination was negative except for slight edema about the eyes and a moderate degree of edema of the ankles. Her urine output in twenty-four hours averaged about 1000 to 1200 c.c., and contained considerable albumin, a few pus cells, an occasional red blood-cell, and a number of hyaline and granular casts. She weighed 119 pounds and the blood-pressure was 110/65. Her heart seemed normal, the peripheral vessels were soft, and the eye-ground study normal. Her hemoglobin was 70 per cent., red blood-cells 4,100,000, white blood-cells 7400. Blood Wassermann was negative. Her phenolsuphonephthalein excretion was 50 per cent. in two hours; the blood-urea nitrogen 22, and the plasma chlorids 742. The specific gravity test showed moderate fixation; the night urine output slightly above normal in amount and low in specific gravity.

Thus the functional studies, other than the excretion of salt and water, showed no great disturbance, and we felt justified in giving a good prognosis in this case of mild renal disease.

We placed the patient upon a diet sufficient to meet her caloric needs, and as there was no reason to greatly restrict her protein, we permitted about 1 gram per kilogram of body weight. However, we did make an effort to restrict the salt and fluid intake. She received 2 to 4 grams of salt a day and 1000 c.c. of fluid. Her tonsils, which were rather large and cryptic, were removed.

She did not do especially well, however, and was permitted to go home in April with but slight, if any, clinical improvement; that is to say there was still considerable edema of the ankles, although she had lost a few pounds, which probably represented a fluid loss. The urine no longer showed red blood-cells and the blood-urea nitrogen had been reduced to 13.

Our patient made no effort to observe dietary rules at home; in fact, she subsisted largely on milk, cream, and eggs. You probably know that milk diets are frequently prescribed in nephritis, but in such a case as this one they do more harm than good; first, milk is high in salt content, and second, far too much fluid must be given in order to provide sufficient nourish-

ment. Therefore a milk diet is wrong in two essential points—it contains too much salt and too much water.

It has recently been suggested by Rockwood and Barrier<sup>2</sup> that the beneficial action of a milk diet in acute nephritis with edema is due to the high calcium content, the calcium acting as

TABLE III.  
A comparison of the findings in Case III.

		February	April	June
Weight		119	111	103
Blood Pressure		110/65	105/68	120/80
Hemo- Globin		70%	65%	75%
Eye Sclerae		Normal	Same	Same
Heart and vessels		Normal	Same	Same
Edema		Moderate	Same	None
Urine	24-hr. output	1,000 to 1200 cc.	Same	1200 to 1400 cc
	Anal- ysis	Heavy cloud albumin, pus cells, occasion- al red blood cells, hyalin and granular casts	Same, except no red blood cells	As before. No red blood cells
Phenolsul- phonethylal- bin		50%		48%
Blood urea nitrogen		22	13	16
Plasma chlorides		742	716	545
2-hr. specif- ic gravity test		Fixation 1004 - 1010 Night urine 400 cc. sp. gr. 1010 Total output 1350 cc.	Fixation 1006 - 1012 Night urine 400 cc. sp. gr. 1008 Total output 925 cc.	Fixation 1004 - 1012 Night urine 350 cc. sp. gr. 1010 Total output 980 cc.
Diet		Salt poor Fluid restriction	Same	Salt free Fluid restriction

a diuretic. But the same authors make mention of the high salt and water content of milk as being an objection to its usefulness in such cases, and suggest that the same amount of calcium be administered after the protein, salt, fluid, and caloric value of the diet have been properly adjusted.

Our patient returned to the hospital in June, in about the same condition as when she left. As you will see in the accompanying table (Table III) comparing her findings then with those in February and April, there was very little difference, except that her plasma chlorids were somewhat lower.

She was again put upon a diet just sufficient to meet her caloric needs in order to make the total burden on the kidneys as light as possible. She was limited to 1000 c.c. of fluid a day, and put upon an absolutely salt-free diet. After following this régime for about three weeks we noted a definite lessening of the edema (she reduced 8 pounds in weight, representing fluid loss) and in another week the edema had entirely disappeared and has remained absent up to the present time.

This case presents a real problem in practice. Here was a young lady who did not suffer, indeed, she felt perfectly well in every respect, except that she was prevented from following her daily routine by a bothersome edema. But for difficulty in the excretion of salt and water her renal function was good, and we felt that we were justified in giving a good prognosis.

What is the basis of dietary adjustment in such a case as this one? First, to relieve the kidneys as much as possible of the job of excreting these particular substances that it finds difficulty in handling, namely, salt and water; and second, to see that the total diet is sufficient to meet the bodily needs and no more.

How shall we do this? Well, roughly, we estimate her caloric needs, at rest, to be about 30 calories per kilogram of body weight, and then give a normally balanced diet to meet these needs. Such a diet is estimated to be<sup>3</sup>: carbohydrate 67 per cent., protein 16 per cent., and fat 17 per cent. of the total calories which will allow about 1 gram of protein per kilogram of body weight.

We must remember that if the kidneys are efficient in the excretion of nitrogen, as determined by functional studies, there is no need to unnecessarily limit the protein intake; in fact, to do so works harm rather than good. This lesson has been pretty well learned by this time; but many a patient has

suffered more from protein restriction than from his renal disease.

And now the problem is to make the diet salt free, and upon our success in this regard depends to a large degree, I believe, the outcome of the case.

You will recall that during this patient's first stay at the hospital salt was only ordinarily restricted, and there was practically no improvement, but on her second admission every effort was made to exclude salt, and it was then that she became wholly free from edema. No one can say with absolute certainty that the element of time did not enter here to bring about improvement, but in view of the later findings, which were about the same as on her first admission, it would seem that the severely restricted salt diet was the responsible factor.

It is especially from Allen, in the treatment of hypertension, that we have learned the valuable lesson of thorough salt restriction. Whether or not we are willing to accept Allen's teachings in regard to the treatment of hypertension with salt restricted diets, we can do no better than obey his instructions in regard to the matter of rendering the diet salt free in such a case as this one.

The salt restricted diet that our dietitian, Miss McInnis, arranged for this patient was made up as follows:

Breakfast:

- A serving of fresh fruit, such as an orange, or
- $\frac{1}{2}$  a small canteloupe.
- 1 shredded wheat biscuit.
- 1 egg.
- 1 slice of bread.\*
- 1 square of butter.\*

Dinner:

- 2 ounces of meat (a small steak, or 2 thin slices).
- 1 medium-sized potato.
- 3 ounces of 5 per cent. vegetables (an ordinary helping).
- 3 ounces of 10 per cent. vegetables.
- 1 slice of bread.
- 1 square of butter.
- 5 ounces of fresh fruit, 1 teaspoonful of sugar.

\*Salt free.



## Supper:

- 2 eggs.
- 1 medium-sized potato.
- 3 ounces of 5 per cent. vegetables.
- 3 ounces of 10 per cent. vegetables.
- 1 slice bread.
- 1 square butter.
- Fruit as at noon.

Upon such a diet we felt that our patient should be salt free, but remember that the method of determining this is to estimate the total salt excretion in twenty-four hours, and unless it is below 1 gram, we have not attained strict salt privation. This patient's excretion varied between 1.9 and 1.2 grams; and although we carefully checked over her diet several times, we were unable to reduce it below this point. Nevertheless her edema disappeared and she has again been returned to her home, with instructions to follow her diet exactly. In view of her prompt improvement, I believe that she will do this, and will have no great difficulty in so doing. The diet can readily be made salt free at home, and kept salt free. Although she still has considerable albumin and casts in her urine, this does not serve as a reliable index to the severity of her lesion, and my feeling is that she will make a fairly good clinical recovery from her present trouble. The probabilities are, however, that a certain amount of residual kidney damage will always leave this patient susceptible to strain, such as pregnancy or infection. She ought to be cautioned in regard to the danger of pregnancy (for the next few years, at any rate) and advised to seek a warm and equable climate, if she can, in order to insure her as far as possible against the common respiratory infections.

The last case that we shall consider today represents a type of renal disease somewhat similar to the one just detailed, in that the functional disturbance is the same, but the pathologic change is a chronic one, and for that reason makes the treatment much more difficult.

**Case IV.**—R. S., a colored man aged thirty-two, born in the Dutch West Indies, but who has lived in Philadelphia since

1910, was first admitted to the Jefferson Hospital September 20, 1922. Swelling of the body was his chief complaint. His family history was unimportant. He did not recall his childhood diseases, but knew that he had never had scarlet fever, and states that he never suffered from any tropical disease. He had recurrent attacks of gonorrhea, and what is more important from the standpoint of his present trouble, since 1915 he has had attacks of tonsillitis every winter. Following such an attack in January, 1922, he became edematous and the edema progressively increased. Later he suffered from headache and dizziness, then became dyspneic, and was admitted to the hospital in September with general anasarca. He weighed  $185\frac{1}{2}$  pounds.

Our studies established the diagnosis of kidney disease. By sweating and purgation he was reduced to  $143\frac{1}{4}$  pounds. Then in November, 1922, after tonsillectomy, he was permitted to leave the hospital, considerably improved, but still showing a moderate degree of edema about the ankles.

During this first admission (after his edema had been greatly reduced) we established that his heart and vessels were normal; eye-grounds normal; blood-pressure 130/80. The blood-urea nitrogen was 19, and the phenolsulphonephthalein excretion 60 per cent. In the specific gravity test there was fixation at a high level, and a small amount of night urine. The blood Wassermann was negative; the urine contained a cloud of albumin and a number of hyaline and granular casts. From a functional standpoint at this time his lesion was similar to that of the young woman of whom we have just spoken.

In March, 1923 (four months later) he was readmitted to the hospital, badly swollen (weight 171 pounds) following a "cold." His blood-pressure was 150/90; blood-urea nitrogen was now 42. The specific gravity test now showed fixation at a lower level than before and the night urine was larger in amount. From these facts it would seem that his renal lesion was undergoing a progressive change, and that now he had some difficulty in excreting nitrogen as well as salt and water.

He was treated as before, but did not respond as promptly, and in June (three months later) he was allowed to go home.

He then weighed 154 pounds and still had considerable edema of the feet and ankles. From this time on to his third admission (November, 1923) he was never free of edema, and it was upon this admission that he promised co-operation in a determined effort to rid him of the edema. He now weighed  $214\frac{1}{2}$  pounds, which represented the largest amount of edematous fluid that he had ever accumulated. His blood-pressure was 200/144; blood-

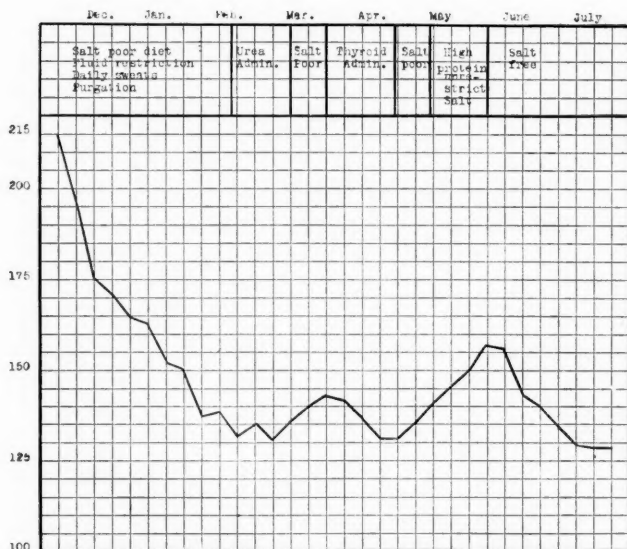


Fig. 152.—Showing weight (edema) variation in Case IV.

urea nitrogen 34; plasma chlorids 495; and the phenolsulphonaphthalein output (intravenous) 15 per cent. in two hours.

His treatment was divided into a number of periods, represented in Fig. 152, and will be spoken of in that order.

1. At first he was put upon a well-balanced diet of approximately 2300 calories, with salt restriction and total fluids limited to 1000 c.c. a day; then by means of daily sweats and purging his weight was reduced from  $214\frac{1}{2}$  to 132 pounds in ten weeks—

a loss of  $82\frac{1}{2}$  pounds. His blood-pressure at the same time fell to 120/80.

2. For the next period (February 4th to March 1st) the sweating was continued every other day; the diet and fluid intake remained the same, and his weight varied but little, although for twelve days in succession he received 15 grams of urea by mouth, with the thought that it might act as a non-harmful diuretic.<sup>4</sup> The blood-urea nitrogen estimated daily during this period gradually rose from 35 to 115, but not a single ill effect was observed. Thus, although this short course of urea administration failed to reduce his edema, it did bring further proof of the innocuousness of large doses of urea administered by mouth.

3. From March 1st to 9th no particular treatment was given, other than the salt-poor diet and fluid restriction, and during this period there was a slight gain in weight.

4. From March 9th to April 3d thyroid extract was given, with the idea, derived from Epstein's work on nephrosis,<sup>5</sup> that this particular form of renal disease might possibly represent a metabolic disorder of nutrition that could be corrected by the administration of thyroid substance. We began with 1 grain three times a day and gradually increased to 5 grains three times a day, which dose he received for the last twelve days of this period. Diet and fluid intake remained the same; there was no sweating or purging. His weight was reduced from 142 to  $132\frac{1}{2}$  pounds during this period. He then developed a slight intercurrent infection, and the thyroid was stopped. Believing that everything that was possible had been accomplished from thyroid administration, it was not resumed.

5. From April 3d to April 24th no treatment of any sort was given, except the same salt-poor diet and fluid restriction. His weight gradually increased from  $132\frac{1}{2}$  to 142 pounds.

6. During the next period, April 24th to May 20th, he was abruptly changed to a high protein, low fat, unrestricted salt diet. On this he did badly. His weight increased from 142 to  $157\frac{3}{4}$  pounds; his blood-pressure rose from 120/80 to 178/26, and the blood-urea nitrogen, which had fallen to 16, rose to 32.

7. On May 26th he went back to his old diet, and now we made every effort to prevent the intake of salt; in other words, instead of a salt-poor diet, we tried to give him one which would be salt free. From a diet list compiled by Allen, only those foods were permitted which contained the lowest amount of salt, which meant that milk was eliminated from the diet (cream diluted with water was permitted as a substitute); bread was prepared without salt or baking powder, and only salt-free butter was allowed. He was given distilled water to drink in place of the tap-water, with the thought that city water might have an appreciable salt content, although the Water Bureau analysis showed an insignificant amount. Estimations were made of the twenty-four-hour salt output in order to check up on the intake. For a time he excreted about  $1\frac{1}{2}$  grams of salt daily, and it was not until we removed meat from the diet (which considerably reduced the protein intake) that we succeeded in reducing his twenty-four-hour output of salt to less than 1 gram, which is the amount that may be considered satisfactory.

Following this plan of rigid dieting and with no other treatment, his weight fell from  $157\frac{3}{4}$  to 129 pounds and there remained only the slightest trace of edema about the ankles. He felt very well, and asked permission to go home, promising to adhere strictly to his diet. His blood-pressure was 140/90; there was no evidence of cardiac enlargement, his peripheral vessels were soft, and the eye-grounds normal. The blood-urea nitrogen varied from time to time, but never went above 60, except during the period of urea administration, his phenolsulphonephthalein excretion was 25 per cent.; repeated specific gravity tests showed a moderate degree of fixation of gravity, with a large output of night urine. The plasma chlorids varied from 400 to 800 mg.; they were low on admission and rose as he rid himself of the edema, later rising when he failed to do well, and falling as he became better, but bearing no constant relationship to his condition. His urine always showed a heavy cloud of albumin, many white blood-cells, and occasional hyaline and granular casts.

His renal lesion might be defined clinically as "chronic nephritis with salt and water, and nitrogen retention—the former predominating."

Three weeks after he had been at home he said that he felt better than he had in two years, and was having no difficulty in keeping his diet salt free. He looked very well and had gained in weight, but this represented solid flesh, because there was hardly a perceptible edema about the ankles. He was advised to get a job in the South for the winter, and to adhere closely to his diet, which is made up as follows:

Breakfast:

- 3 ounces of fresh fruit (10 per cent.), such as an orange or  $\frac{1}{2}$  small cantaloupe.
- 1 serving shredded wheat or oatmeal (shredded wheat contains less salt).
- 1 ounce of cream.
- 1 slice of bread.\*
- 1 square of butter.\*
- Coffee if desired.

Dinner:

- 3 ounces of steak (a small steak or other meat) or
- 4 ounces of fish (no clams, oysters, corned beef, smoked ham or bacon).
- 2 medium-sized potatoes.
- 3 ounces each of 5 and 10 per cent. vegetables, except beets, celery, endive, dandelion, lettuce, spinach, and watercress.
- 2 slices of bread.
- 1 square of butter.
- 5 ounces of fresh fruit (10 per cent.) with a tablespoonful of sugar.
- Coffee or tea if desired.

Supper:

- 2 eggs.
- 2 medium-sized potatoes.
- 3 ounces of a 5 per cent. vegetable.
- 2 slices of bread.
- 1 square of butter.
- 5 ounces of fresh fruit with 1 tablespoonful of sugar (bananas and coconut not permitted).
- 1 ounce of cream.
- Tea or coffee if desired.
- \*Salt free.

By following such a diet I believe that he can remain comparatively well and avoid edema. It is needless to say that he

can never recover completely, indeed, his trouble may return on slight provocation; but we are all well satisfied with the progress he has made, and feel that the last attempt has been successful because of a long-continued rigid salt restriction.

In closing this discussion may I advise you gentlemen who are about to become interns that the only way to learn anything of value about the regulation of the diet in such diseases as nephritis and diabetes is to go into the diet kitchen and receive instruction from the dietitian in food values. Merely to write an order for a diet of say, carbohydrate 70, protein 50, and fat 120 will teach you nothing, unless you go into the diet kitchen and choose the articles of food, weigh them out yourself, and see what they look like when assembled.

I do not want you to get the idea from our discussion of treatment that weighed diets are necessary in nephritis; we have used them because we were dealing with hospital cases and desired to be exact. But I want you to realize equally well that any method of dietary adjustment which consists of telling your patient to "drink only milk" or to "cut out meat and eggs" is both unscientific and bad practice.

I need hardly say to you that drugs are of little value in the treatment of such cases as we have discussed. Mild diuretics may be used more for their effect upon the patient's mind than upon his kidneys, for, while they are probably harmless, I doubt that they do very much good; severe diuretics are unquestionably harmful. A sound understanding of the pathology of nephritis, a sensible appreciation of the altered physiology, and some knowledge of dietary principles will always remain the basis for the satisfactory treatment of kidney disease.

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## CLINIC OF DR. JOHN H. ARNETT

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### THREE CASES ILLUSTRATING THE VALUE OF VITAL CAPACITY CHARTS IN DISEASES OF THE HEART, LUNGS, AND MEDIASTINUM.

WHEN an individual breathes naturally, the quantity of air moving in and out of the respiratory passages is known as the "tidal air." When, however, respirations are forced to their maximum depth we have what is known as the "vital capacity." Accurate measurements of these phases of respiration were first made by Hutchinson<sup>1</sup> by means of a water spirometer which he himself designed. He studied upward of 2000 persons, and published his findings in an article which in its field has never been excelled. Hutchinson believed that the spirometer was destined to become an instrument of value in the diagnosis and study of pulmonary diseases. That his belief was not without foundation is evidenced both by the material presented by him, and also in the fact that recently we have turned again to the spirometer in the study of problems connected with respiration.

The greatest impetus which vital capacity has received since Hutchinson's time was given by the studies of Peabody<sup>2</sup> and his associates, who pointed out that a very definite relationship exists between the degree of cardiac decompensation and the degree of vital capacity diminution. Following the studies of this Boston group, some of which have been reported in the Medical Clinics of North America,<sup>3</sup> many reports dealing with this subject have been published from widely different sections

<sup>1</sup> Hutchinson, J., *Med. Chir. Trans.*, 29, 137, 1846.

<sup>2</sup> Peabody, F. W., and Wentworth, J. A., *Arch. Int. Med.*, 20, 443, September, 1917.

<sup>3</sup> Peabody, F. W., *Med. Clin. N. America*, 4, 1655, May, 1921.

of the country. It may be said that in spite of the differing conclusions which various workers in the field have drawn, nevertheless the data from which these conclusions were deduced are, on the whole, in fairly close agreement. It has been possible, therefore, from published protocols to reach a fairly well-grounded view of the value of vital capacity as a clinical procedure.<sup>1</sup>

From the standpoint of ease of determination the vital capacity leaves little to be desired. The patient simply takes the deepest possible inspiration and exhales to his fullest capacity into the mouthpiece of the spirometer. The reading is made directly from the dial of the instrument. The hands are again set to the starting-point and the procedure repeated as often as may be necessary in order to assure accuracy. Here, then, is a very simple procedure, suitable for a physician's private office or a hospital ward. The value of the procedure in following the clinical course of patients with diseases of the chest is well illustrated by 3 cases from the Medical Service of the University Hospital, being types of cardiac, pulmonary, and mediastinal disease.

**Case I.**—The first patient, W. B., a white male of thirty-six, had been operated upon for a bilateral inguinal hernia twenty-two days before his present admission. The operation required a fascia lata transplant. Four days later a cough developed and a friction-rub was heard at the base of the right lung. The rub was soon replaced by signs of fluid. The physical signs rapidly cleared up however, and the patient was sent home, but less than an hour after his discharge he was suddenly seized with a severe pain in the chest. He was now admitted to the medical service of the hospital. Thrombosis of the saphenous vein of the right leg was discovered, which apparently had followed the operation. The chest examination suggested a localized collection of fluid at the base of the right lung, and the x-ray corroborated this finding. The diagnosis of pulmonary

<sup>1</sup> Arnett, J. H., and Kornblum, K., *Annals of Clin. Med.*, 3, 225, October, 1924.

infarct was made, the patient was put in the Fowler position, the intake of fluid was limited to 1200 c.c. per day, and further developments were awaited. An uneventful recovery took place (see Fig. 153) and the patient was discharged in satisfactory condition.

Here a single vital capacity determination did not assist in differentiating the various pulmonary complications which were

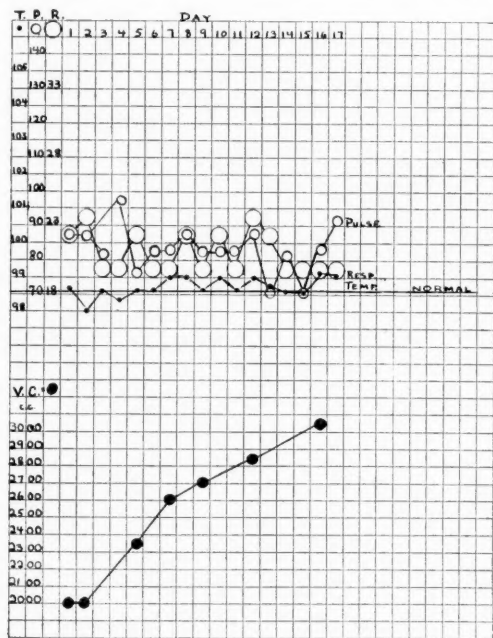


Fig. 153.—Vital capacity and clinical chart of Case I, diagnosed pulmonary infarction following herniorrhaphy. The normal line applies only to pulse, temperature, and respiration.

under consideration, *i. e.*, pneumonia, pleurisy, infarct, and pulmonary collapse. It simply indicated that an individual who from his height should have possessed about 5000 c.c. of vital capacity actually possessed two-fifths of this quantity. The diminution might have been caused by any one of several lung

conditions, or might have equally well been due to cardiac or mediastinal pathology. However, repeated determinations showed a steady improvement, which argued for an evanescent and acute process rather than a chronic one. This improvement was not well evidenced by the temperature, pulse, and respiration graphs. The general appearance of the patient, and the blood-picture also helped very little in this case, so that here the vital capacity proved of distinct value in following the clinical course of the patient.

**Case II.**—Figure 154 shows the chart of W. S., a white male, aged forty-one, who complained chiefly of swollen glands and shortness of breath. The swelling was first noted three years ago in the right axilla, but gradually involved the other lymph-nodes as well. When admitted to the hospital the cervical lymph-nodes and the parotid salivary glands stood out like hens' eggs. The lymph-nodes of the entire body were likewise markedly enlarged. The patient's face was of a somewhat cyanotic hue, he coughed considerably, and had evident difficulty in breathing deeply. The area of supracardiac dulness was widened in extent and the veins of the right upper chest stood out prominently. We had every reason to believe, therefore, that the mediastinal glands were involved in the general lymphadenopathy, and x-ray plates of the chest corroborated this view. Blood studies failed to assist in differentiating Hodgkin's disease, lymphosarcoma, and aleukemic leukemia, which from the physical findings were regarded as the most probable diagnoses; consequently one of the cervical lymph-nodes was excised under local anesthesia. Dr. Herbert Fox examined sections of this tissue and reported lymphosarcoma. x-Ray treatment was then administered, a full erythema dose being given over all areas of glandular enlargement, including the mediastinum. This was followed by radium treatment of half of an erythema dose over the superficial glands. Improvement was marked and immediate. Breathing became easier, coughing grew less, the superficial lymph-nodes diminished visibly day by day, and an x-ray of the chest showed considerable clearing of the mediastinal shadow. The

patient was discharged with instructions to return in one month for more radiation.

The temperature, pulse, and respiration graphs failed utterly to indicate the sudden and almost miraculous improvement which took place in this patient's condition. The x-ray plates

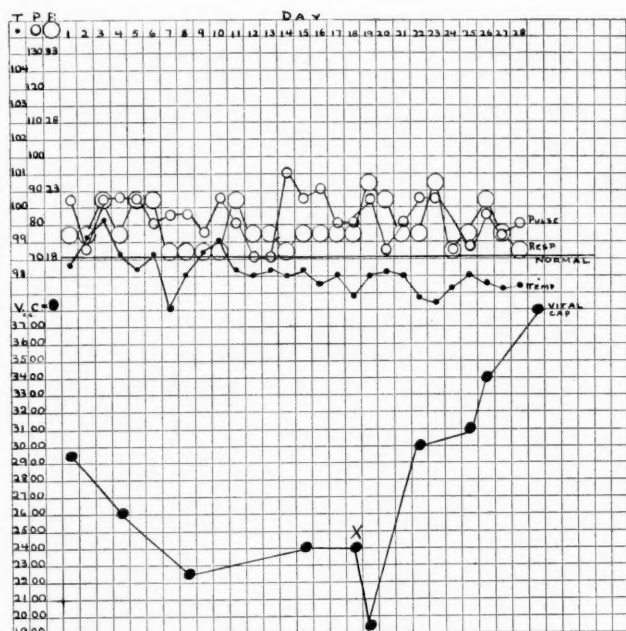


Fig. 154.—Vital capacity and clinical chart of Case II, diagnosed lymphosarcoma with mediastinal involvement. x-Ray treatment of mediastinal glands begun at X. The normal line applies only to pulse, temperature, and respiration.

of the chest showed it better, but short of seeing the patient face to face day by day the vital capacity graph gives the best visualization of his clinical course. It shows a gradual fall of the vital capacity as his cough and breathing became worse, with a precipitate drop after exposure of the mediastinal glands to x-ray, the vital capacity at this point being about one-half of what a

man of his height should possess. It shows the rapid rise coincident with his clinical improvement. The vital capacity chart was therefore of definite value in following the effects of treatment in this case of lymphosarcoma with mediastinal involvement.

**Case III.**—The third patient, A. C. M., is a white male aged twenty-one, who is convalescing from an attack of acute rheumatic fever and endocarditis. The flushed face, heaving cardiac impulse, and pulsating carotid vessels make the diagnosis of aortic regurgitation seems probable from inspection. Careful examination bears out this diagnosis, and reveals, in addition, acute articular rheumatism of the left lower extremity. Enormous cardiac enlargement, and all the peripheral signs of aortic regurgitation are present.

The clinical course of this patient has been long and stormy. Being of a neurotic temperament he has been subject to attacks of extreme apprehension and dyspnea, which at times have required morphin for their relief. A gram of sodium salicylate four times daily was given for a few days for the joint condition. Digitalis and sedatives were freely used throughout. He is now about to leave the hospital for a convalescent home, greatly improved, but still subject to occasional attacks of nervousness and dyspnea, and with the menace of cardiac decompensation constantly in the background.

A study of his chart (see Fig. 155) is of interest from several standpoints. It will be noted that the vital capacity was low during the period of his greatest illness, and that even before the pulse, temperature, and respiration showed any marked improvement the vital capacity had commenced to increase. This increase was coincident with a general subjective and objective improvement. From the standpoint, therefore, of visualizing the clinical course of the case, the vital capacity graph is here a valuable adjunct.

We see, therefore, that in diseases of the heart, lungs, and mediastinum we may have a very marked reduction of the vital capacity, and that therefore this determination cannot be

used to make a differential diagnosis between these three conditions; neither can it be used to diagnose the particular pathologic processes which may involve the heart, lungs, or mediastinum.

You will perhaps have noted that very little has been said

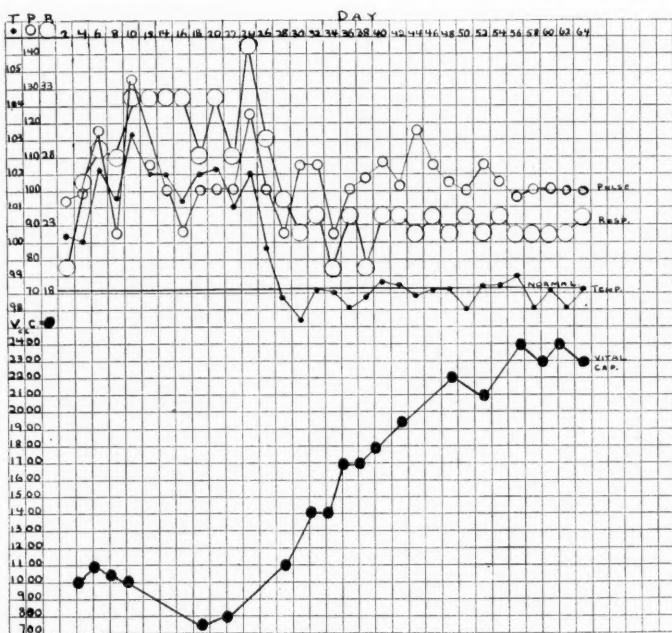


Fig. 155.—Vital capacity and clinical chart of Case III, diagnosed acute rheumatic endocarditis, aortic regurgitation, decompensation. One division represents two days. The normal line applies only to pulse, temperature, and respiration.

regarding standards. This omission has been deliberate. Vital capacity standards, when applied to healthy individuals living under relatively uniform conditions, show variations of such frequency and degree that even the best standard must be regarded as a very inaccurate estimation of the vital capacity which a

healthy person should possess. Hewlett and Jackson,<sup>1</sup> for example, in a series of 400 normal students at Leland Stanford Jr. University, found readings which ranged from about 30 per cent. below to about 30 per cent. above the standard used. Myers and Myers,<sup>2</sup> in a series of 1280 female students, also report frequent and wide variations from the standard. Since age, race, occupation, and habits of exercise are known markedly to influence the vital capacity, one would expect even greater variations to occur among patients in a hospital ward. Such has been our experience. Lemon and Moersch,<sup>3</sup> in a study of 329 patients free from pulmonary or cardiac disease, found 174 whose vital capacity readings were below the estimated normal. The degree of reduction in the average case amounted to 14 per cent.

With vital capacity reductions of this magnitude occurring in persons without cardiac or pulmonary disease, it is obvious that in order to be of diagnostic significance a much greater reduction than 14 per cent. is required. We must, therefore, regard our vital capacity standards as extremely rough and inaccurate means of estimating a person's normal vital capacity, and by the same token we must admit that our present standards possess a very limited value in the diagnosis of diseases of the chest.

However, it is often valuable to have a rough estimation of what the vital capacity in a given case should be. For this purpose I believe a standard based upon height alone is more satisfactory than one based upon weight, either alone or combined with the height, as in West's surface area standard, for example. This is true because this surface area standard assumes a normal relationship between height and weight, which in many patients in a hospital ward does not exist. For example, two very common conditions producing a diminution of the vital capacity are pulmonary tuberculosis and cardiac failure. In one there is frequently emaciation, and in the other edema and anasarca.

<sup>1</sup> Hewlett, A. W., and Jackson, N. R., *Arch. Int. Med.*, 29, 515, April, 1922.

<sup>2</sup> Myers, J. A., and Myers, F. L., *Journal-Lancet*, 42, 519, October 15, 1922.

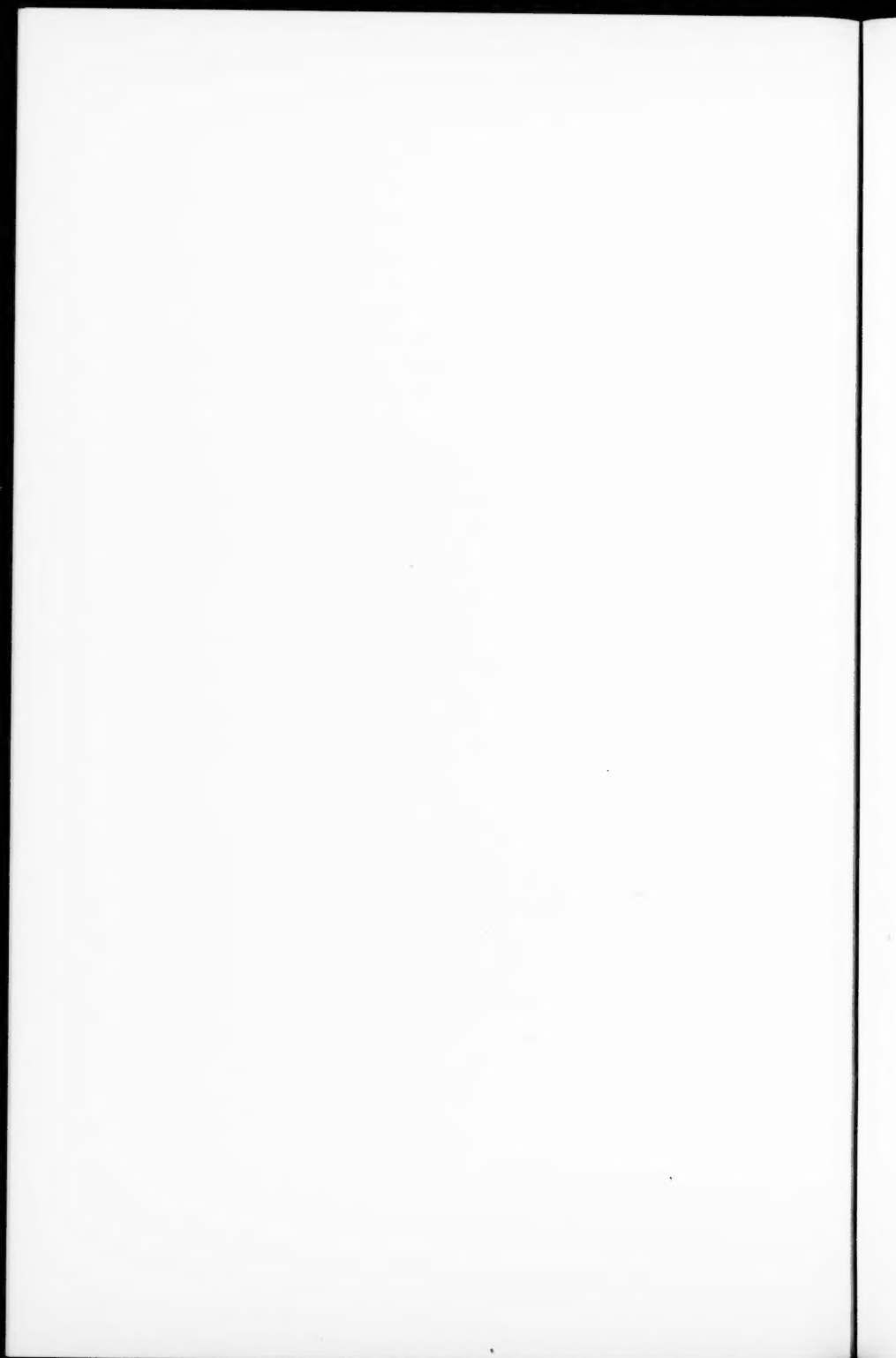
<sup>3</sup> Lemon, W. S., and Moersch, H. J., *Arch. Int. Med.*, 33, 118, January, 1924.



The weight, therefore, throws a confusing element into the standard. Furthermore, since simplicity is always an important factor, it seems more rational to use a simple height formula, such as recommended by Peabody and Wentworth, West,<sup>1</sup> or Hewlett and Jackson. Be that as it may, the important thing to remember about vital capacity standards is their unreliability, unless applied only to the group from which they were derived. For example, standards derived from American students are wholly inadequate for accurate work upon ward patients, and are even too high for English students.

Aside from the question of standards, however, the vital capacity possesses a definite value in following the course of patients with diseases of the chest; it offers likewise a method of studying their pathologic physiology. Furthermore, by watching the vital capacity of our private patients from year to year a sudden reduction, which cannot be otherwise accounted for, may perhaps be a valuable early indication of incipient pulmonary disease.

<sup>1</sup> West, H. F., Arch. Int. Med., 25, 306, March, 1920.



CLINIC OF DR. THOMAS FITZ-HUGH, JR.

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**SYPHILIS AS A CAUSE OF DELAYED RESOLUTION IN  
PNEUMONIA**

FROM the very beginning of our medical student days we are constantly reminded of the manifold, protean, and devious manifestations of syphilis. There are very few lists of "possible causes" of our many medical mysteries that do not include the ubiquitous syphilis. So frequently is this cry of "wolf" heard by the student that sometimes—especially in his fourth year or in his intern period—it fails to arouse his skeptic interest. And yet Sir William Osler said "Know syphilis in all its manifestations and relations and all other things clinical will be added unto you."

I wish today to call to your attention the subject of syphilis as a factor in the so-called delayed resolution in pneumonia. This phase of syphilis in relation to pneumonia is not mentioned in any of the standard text-books or systems of medicine that I have been able to discover, although syphilis of the lung (supposedly unrelated to acute pneumonia) now occupies an important place in the literature of pulmonary diseases.

Delayed resolution in pneumonia, according to Osler, occurs in from 3 to 4 per cent. of cases. In making this diagnosis, however, the physician must be constantly on guard to rule out the other more common and important complications, such as pleural effusion, empyema, lung abscess, and an underlying pulmonary tuberculosis. To these should be added syphilis, which is at least one important cause of so-called delayed resolution, as the following cases will illustrate.

**Case I.**—Mrs. H., a white woman of forty-seven years, was admitted to the University Hospital, service of Dr. Alfred Stengel, on February 28, 1923. She stated that she had been in good health until about a week before admission when she "caught a slight cold" and felt feverish, but continued to perform her usual household duties until four days before admission. At this time, after some exposure to inclement weather, she had a chill, severe headache, pain in her left chest, and increased

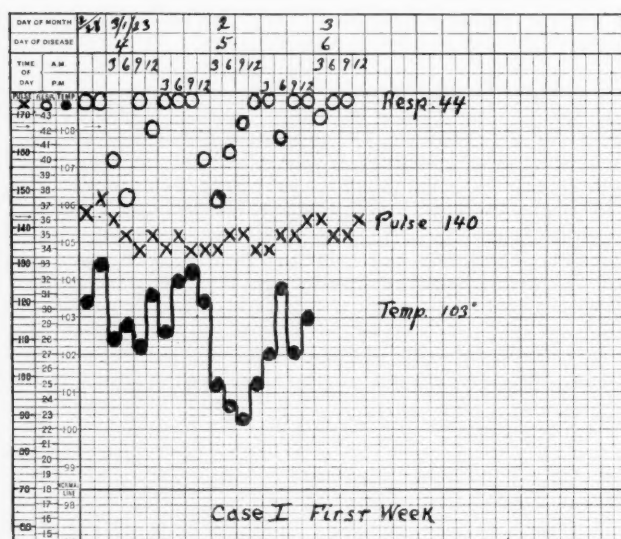


Fig. 156.—Case I. (Copy of Clinical Record.)

cough. Her previous medical history was quite uneventful. She had been pregnant only once, resulting in premature delivery at the seventh month, the child living twenty-four hours. She had never had a chronic cough or hemoptysis. She had suffered from severe headaches during the month prior to her present illness. Her father was said to have died of tuberculosis. One sister had a stroke at about forty years of age. She and her husband had separated. Her living conditions were poor.

Physical examination on admission revealed the usual evidence of an acute pneumonia of the lobular type. The patient was very ill, with flushed, hot skin, orthopnea, suppressed cough, and the characteristic expiratory grunt. There was dullness on percussion over both pulmonary bases posteriorly. The breath and voice sounds were tubular, and there were many resonating subcrepitant râles over these consolidated portions of the lungs. The heart was slightly enlarged to the left and was beating at a

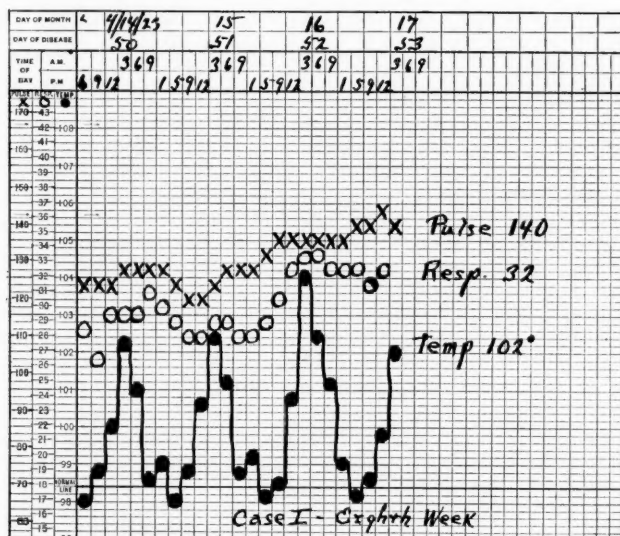
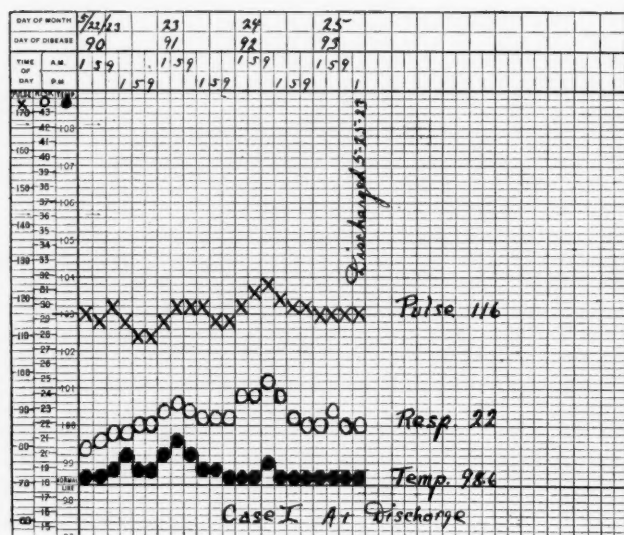


Fig. 157.—Case I. (Copy of Clinical Record.)

rate of 140, but was otherwise negative. On admission her temperature was 103.2° F., respirations 44, pulse 140, and blood-pressure 120 to 70. Her leukocytes were 15,000, of which 84 per cent. were neutrophils. Sputum contained Type IV pneumococcus. The obvious diagnosis was acute bronchopneumonia (Fig. 156).

Her subsequent course was marked by prolonged, hectic fever, with night-sweats, circulatory failure, dicrotic pulse, nocturnal

delirium, and very striking persistence of pulmonary signs. Involvement of both pulmonary apices became evident about the fourth week. At the same time the signs at the left base changed from those diagnostic of consolidation to those suggesting effusion. Thoracentesis was performed in the confident expectation of finding purulent fluid, but none was obtained. An x-ray picture was made at this time (Fig. 159) which strongly suggested tuberculosis. By this time about a dozen examinations



and seemed doomed to die, when about the end of the eighth week of her fever it was noted that the routine Wassermann had not been made. This was done at once and was reported strongly positive in all three antigens. The temperature chart shows the character of the fever at this time (Fig. 157). The

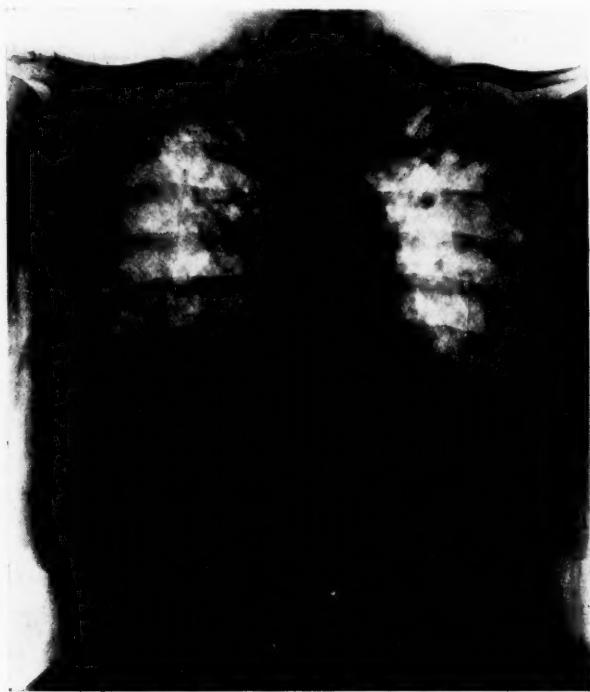


Fig. 159.—Bedside plate 3/13/23. Dr. Pancoast's report: "Probably tuberculous process of both apices. Lesion at both bases may be bronchopneumonia or extension of tuberculous process."

x-ray (Fig. 160) was taken also at this time before antiluetic treatment was started. On the fifty-sixth day of her fever the patient received her first mercurial inunction and her first dose of iodids by mouth. This form of treatment was continued for two weeks until ptyalism developed when neo-arsphenamin was

given instead in the usual way. The improvement was very striking indeed and was noticeable within two or three days after the antiluetic régime was instituted. More or less steady progress toward recovery continued and the patient was dis-

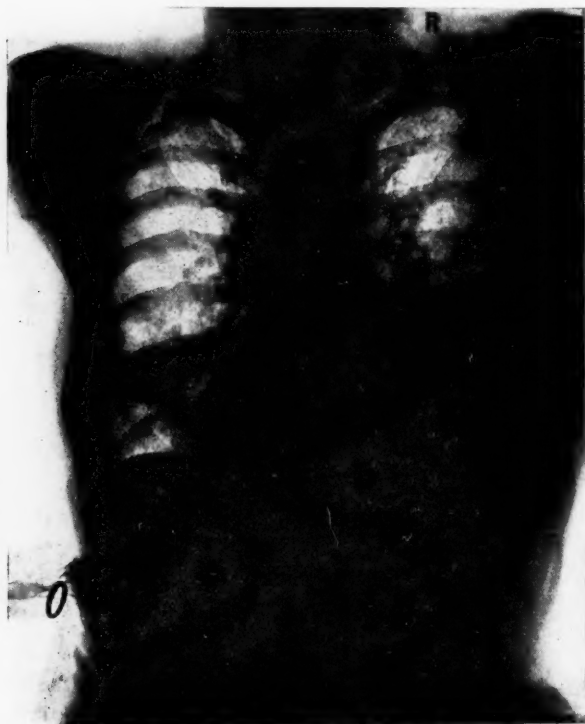


Fig. 160.—Stereoscopic plates 4/19/23. Dr. Pancoast's report: "Evidence of old tuberculous process in each apex. Lesion right lower lobe either localized collection of fluid or consolidation. Lesion left base, identity uncertain. Gumma of one or both bases to be considered."

charged on the ninety-third day after the onset of her fever in comparatively excellent condition. As may be seen from the chart (Fig. 158) her temperature was normal, but tachycardia and a slight tachypnea persisted. Also a slight cough persisted



at time of discharge which, together with some weakness, constituted the only abnormal symptoms. The physical signs, however, were surprisingly little changed and the x-ray taken the day the patient left the hospital (Fig. 161) is hardly different from



Fig. 161.—Stereoscopic plates 5/25/23. Dr. Pancoast's report: "Appearance about the same. Fluoroscope showed right diaphragm fixed."

that taken before antiluetic treatment had been given and at a time when the patient was in desperate condition (Fig. 160). A second blood Wassermann made at time of discharge was still strongly positive. The sputum continued to be negative for tubercle bacilli.

**Case II.**—Mr. C., a white man of sixty-five, was admitted to the University Hospital, under my care, on April 24, 1924. He was then apparently in the fifth day of an acute pneumonia. He was cyanosed, orthopneic, and at times delirious. Physical signs were typical of lobar pneumonia of the left upper lobe. A striking feature in these signs was the succulent character of the râles over the affected lobe. Leukocytes on admission were 30,000; temperature was 101.4° F., respirations 32, and pulse 100. The sputum contained Type IV pneumococcus. Additional findings were slight anisocoria—the left pupil larger and more sluggish than the right—and a definitely enlarged and tender liver. The patient received the usual stimulative treatment and improved until the twelfth day, when the temperature went up again and a patch of consolidation appeared at the right base. The signs at this right base changed suddenly from day to day—succulent râles and tubular breathing giving place to almost absent breath and voice sounds and flatness on percussion. Just as in the first case previously mentioned, so here, thoracentesis was performed in the expectation of finding fluid, but none was obtained. Eight sputum examinations for the tubercle bacillus were negative.

On account of the unfavorable progress of the patient, with hectic fever, sweats, and somewhat suggestive physical signs (including the enlarged liver) it was thought that this too might be a case of pneumonia prolonged by lues. A Wassermann test of the blood taken May 20th was strongly positive, and antiluetic treatment was instituted at once. The improvement in symptoms was striking and the fever rapidly subsided. The patient was discharged from the hospital, feeling quite well, on May 26th. Physical signs, however, persisted with very little change—the lobes previously affected were still very dull on percussion and resonating râles were still audible. The liver too was still enlarged three fingerbreadths below the costal margin and still tender. It should be said that this patient was the father of two sons—both now apparently healthy adults. His wife was said to be partially blind in one eye. She had one miscarriage—her last pregnancy. The patient's personal history

included gonorrhea and a penile sore at about twenty years of age, for which he took medicine by mouth for a year. He had had a chronic cough for twenty years, which he called a cigarette cough. No hemoptysis.

On a recent visit to the patient's home it was found that the pulmonary lobes previously affected were still dull on percussion and the breath sounds over them were still distant, but the râles had practically disappeared and the liver was much smaller and not tender at all. This was three weeks after antiluetic treatment was started. The patient stated that he felt fine and the cough which he had had so long was entirely absent. He had returned to business. He refused to have another blood-test and an x-ray.

**Case III.**—Mrs. H. O., a negress of thirty-eight years, was admitted to the wards of the University Hospital on April 3, 1923 apparently in the third week of a subsiding pneumonia of the right lower lobe. There was slight fever and the patient did not appear very ill. Signs at the right base suggested a resolving pneumonia with slight effusion which was found to be serous when removed by thoracentesis. x-Ray showed an area of unresolved pneumonia at the right base and no evidence of tuberculosis. Several sputum examinations were negative for the bacillus of tuberculosis and the pleural fluid was sterile on culture and produced no effect on guinea-pigs which were inoculated with it. She showed no improvement until ten days after admission, when, after a positive Wassermann report was received on her blood, antiluetic treatment was instituted. A week later, about six weeks after onset of her pneumonia, she was discharged subjectively well. A second Wassermann taken just before she left the hospital was still strongly positive. The effusion which recurred partially after thoracentesis was apparently entirely absorbed and only slight dulness persisted over the affected lobe.

**Discussion.**—Here, then, are 3 patients who had frank pneumonia, in all of whom the disease ran a prolonged course suggesting so-called delayed resolution; all 3 were syphilitic.

and all were greatly benefited, as regards the pulmonary symptoms, by antisyphilitic treatment. A number of questions arise for consideration: First, did these patients have chronic pulmonary syphilis before their pneumonia, or did the pneumonia determine the localization of truly luetic lung lesions, or did the systemic syphilis in some way cause non-specific true delayed resolution? Second, is it possible that these patients had a true acute syphilitic pneumonia from the start?

The first question cannot be answered on the basis of our knowledge of this problem. We do know that syphilis of the lung, like pulmonary tuberculosis, may be practically symptomless for a time. Case I, therefore, might have had gummata in both lungs which were not discovered until pneumonia was superimposed. It hardly seems credible however. Case II may have had luetic tracheobronchitis for twenty years prior to his acute pneumonia, but it is certain that the consolidation of the right lower lobe developed under our observation, and it was here that the delayed resolution was most marked; hence this lesion at least could not have been a pre-existent luetic one. According to Dr. Piersol,<sup>1</sup> in an article on unresolved pneumonia, "It is highly probable that many cases of so-called pulmonary syphilis are, in reality, instances of postpneumonic delayed resolution occurring in syphilitic subjects, in whom the pulmonary lesion clears up only after the underlying general infection is treated." True pulmonary syphilis as now recognized, however, *does not* clear up entirely even after years of treatment, as judged both by physical signs and by x-ray findings.

It seems to me that an acute pneumonia in a syphilitic subject might readily determine the localization of a truly syphilitic lesion in the damaged lung tissue, which if treated promptly might be expected to clear up in time, but if left untreated until scar formation occurred would probably be permanent. This view, if correct, would harmonize the opinion advanced by Dr. Piersol with the prevailing opinion as to the permanency of true pulmonary syphilis. It seems to fit the facts of the cases just reported. If true, it would emphasize the importance of the

<sup>1</sup> The Penna. Med. Jour., vol. xxv, 1921-22, p. 255.

early recognition and early specific treatment of these cases of pneumonia in syphilitics.

In regard to the second question it is agreed by most authors that true exudative syphilitic pneumonitis never occurs except in the form of the white pneumonia of congenital syphilis in the newborn. Stanley,<sup>1</sup> however, states that a fairly rapid, "gelatinous," infiltrative, acute interstitial pneumonia in adults with tertiary lues, has been observed by him postmortem. He believes this form of pneumonia was truly a syphilitic one. Another report which should be mentioned in this connection is that of Floyd<sup>2</sup> who describes a case of "probable syphilitic interstitial pneumonia in an adult." More studies of this kind, with carefully elaborated clinicopathologic data, will help to solve many of the problems inherent in this subject.

The specificity of the Wassermann reaction, even in the presence of an acute febrile illness such as pneumonia, is now generally admitted. It is the conviction of clinicians and serologists alike that a properly performed Wassermann test, when strongly positive, in the absence of yaws and leprosy, is diagnostic of syphilis. The old ideas concerning "false positives" in pneumonia, malaria, scarlet fever, etc., are now believed to have been based on the results of crude and faulty serologic technic. Dr. Kolmer's articles and teachings on this subject are known to all of you.

Now let us consider the probable frequency of syphilis as a cause of what clinically is delayed resolution in pneumonia. The literature contains little information about it. In the discussion of Dr. Piersol's paper mentioned above, Dr. Simonton, of Pittsburgh, said, "I wish to speak of one kind of case that has come under my observation—unresolved pneumonia in syphilitic subjects. I have had 3 cases of this sort within the last year in which persistent temperature was one of the features. . . . The points that impressed me were the marked consolidation, bronchial breathing, and a tendency to change in the character of the sputum. . . . One important thing

<sup>1</sup> Brit. Med. Jour., vol. 11, 1911, p. 802.

<sup>2</sup> Proc. N. T. Path. Soc., 1921, xxi, p. 58.

was the degree of involvement and very little cough. . . . With massive doses of mercury given by inunction it was surprising how the temperature came down by lysis."

Aside from the brief statements of these two authors, the only other reference to the subject that I have been able to find is a communication by Head and Seabloom<sup>1</sup> in which they report 3 cases, and emphasize the value of arsphenamin. To Head and Seabloom should belong the credit of first calling attention to this important subject.

That syphilis may cause delayed resolution in pneumonia more frequently than the lack of literature concerning it would indicate may be inferred from the following figures. These are based on too few cases to be of decisive statistical value, but serve to show what may happen in an unselected group of pneumonias in ward practice. Last year I reviewed the case histories of 50 consecutive acute pneumonia patients admitted to the University Hospital during the year. Four of these had strongly positive Wassermanns. One of the 4 is the case of Mrs. H. previously described. Another is the case of Mrs. H-O. also described. The other 2 of these 4 were apparently regarded as "false positives" and did not receive specific treatment. One of them ran a stormy and prolonged course of six weeks, and on discharge still exhibited physical signs of residual consolidation, although subjectively he seemed fairly well. The other untreated case apparently passed through a lobar pneumonia with very little evidence of delayed resolution, leaving the hospital in twenty-five days as "cured." Here then are 5 cases of pneumonia with positive Wassermanns, 4 of whom had delayed resolution, and 3 of whom were quite dramatically improved by antisyphilitic treatment.

That pneumonia in a syphilitic is not always complicated by delayed resolution is suggested by the one case above mentioned. Indeed, it would seem probable that the type of syphilis confined to the central nervous system would hardly cause the visceral complications of delayed resolution. This probability,

<sup>1</sup> Arsphenamin in Pneumonia with Delayed Resolution in Syphilitic Soldiers, *Jour. Amer. Med. Assoc.*, vol. lxiii, pp. 1344, 1345, 1919.

however, does not detract at all from the importance of recognizing and treating those cases of delayed resolution which are caused by syphilis.

The *modus operandi syphiliticus* exhibits certain suggestive analogies in other phases of pathology which seem to me to be germane to the subject under consideration. It is generally believed that syphilis is responsible in some way for many cases of delayed or faulty union of fractured bones. Local injury in an already syphilitic subject may determine the development of a syphilitic lesion at the site of injury, as may be ascertained by a review of some recent medicolegal cases. The same factor is thought to be the cause of leukoplakia—*i. e.*, irritation of the tongue from tobacco in an individual who has systemic lues. Recently I have read that a prolonged painful pharyngitis following tonsillectomy should always arouse suspicion of lues. If these analogies be valid, is it not reasonable to expect something similar in the damaged lung substance of syphilitics with pneumonia?

By way of summary I would emphasize the following points:

1. Syphilis is an important cause of what clinically is delayed resolution of acute pneumonia. It is more frequent than is generally recognized, and deserves a place in our textbooks along with effusion, empyema, lung abscess, pulmonary tuberculosis, and the other well-known complications and sequelæ of pneumonia.

2. The report of a positive Wassermann test, made by a competent serologist, is indicative of syphilis even when the blood is tested during the course of an acute pneumonia. But a patient may have syphilis and empyema too.

3. A pneumonia patient, whose febrile illness is unduly prolonged by persistence of pulmonary pathology and in whose case empyema, abscess, and tuberculosis can be reasonably well excluded, should have the benefit of a Wassermann test. If this is positive the patient should have vigorous antiluetic treatment. The therapeutic test completes the diagnosis from a practical standpoint at least.

4. In addition to the "diagnosis by exclusion," supplemented

by the Wassermann test and the therapeutic test, the complete diagnosis would seem to be *suggested* by the following: (a) Rapidly changing physical signs elicited over the involved lung tissue, which one day might seem to be the site of massive effusion and the next day clearly in a state of marked consolidation with loud tubular breathing and succulent râles. (b) Evidence of visceral syphilis in other organs—*e. g.*, an unduly enlarged and tender liver. (c) A history indicative of syphilis. (d) The x-ray picture.

5. Finally it is suggested that if syphilis is constantly borne in mind by all who have to treat pneumonia, this complication will be recognized and combated at an early stage, when gratifying results can be obtained. It seems probable that by early treatment of this form of delayed resolution some patients will be spared the indelible lung scars that in after years would surely be dubbed "syphilis of the lung."



## CLINIC OF DR. RALPH M. TYSON

JEFFERSON HOSPITAL

### THREE CARDIAC CASES

FROM a fairly large group of cardiac cases I have selected three to talk about. They are of more than casual interest and have proved very instructive. The first case is unusual because of the early age at which rheumatic manifestations occurred. These manifestations rarely occur before the third year, and only a few cases are reported which developed before the fifth year. In the following case a very clear history gave the onset at twenty-six months. The cardiac lesion was not discovered until the child was four years old.

**Case I.**—Sylvia S. This child was brought to the clinic shortly after her fourth birthday because the family physician found a "leaking heart." At twenty-six months of age she had pain and swelling in both feet and for a short time refused to walk. The child was not confined to bed. It seems reasonable to believe that the severity of the cardiac disturbance in the mild rheumatic cases can be accounted for by the fact that the patient was not confined to bed and the heart put at rest. Two years later an examination by the family physician revealed the murmur. At that time the little girl weighed 38 pounds and was 39 inches tall. She was well nourished. There were no symptoms of cardiac disease. The apex-beat was found in the fifth interspace just inside the nipple line. A thrill was not felt. The impulse was more forceful than usual. The transverse diameter of the heart was 9 cm. At her age 7 cm. is considered the normal diameter. A very musical systolic murmur was heard at the apex and in the axilla, both sitting and lying. The

systolic blood-pressure was 92, the diastolic 60. The heart-rate lying was 116 per min. After 50 hops the rate was 150 per min. In two minutes it returned to 104 per min. There was slight flushing of the face and slight breathlessness following this exertion. A number of badly decayed teeth and diseased tonsils were removed. No restrictions were placed on her activity. A generous diet was urged. During the three years she has been under observation her weight has increased to 55 pounds, her height to 47 inches. The murmur has changed to a soft blowing systolic one; her heart has not increased in size. At the present time according to her size the heart is normal in diameter. The prognosis is good. Since the foci of infection have been removed, and there has not been any evidence of cardiac infection in three years, the child will probably outgrow any defect, and even the murmur may disappear.

**Case II.**—Floyd S. At the age of four this boy was brought to the cardiac clinic because of nervousness and twitching. He had had measles at two years, pertussis at three years, and some illness several months before his admission. This illness was stated to have been influenza and "cold in the throat." The nervousness began three weeks before admission and about one month after the last illness. The child was irritable and had a bad disposition according to the mother. On admission his temperature, pulse, and respirations were normal. His weight was 38 pounds. There was some mild twitching. His nutrition was good. The tonsils were small and apparently not diseased. There was no cervical adenitis. A systolic murmur was heard at the mitral area. The heart was normal in size and had a normal exercise tolerance. The child was lost sight of for one year. Upon his return the mother stated that the twitching soon disappeared and that he seemed normal. About two weeks prior to his return he had an attack of rheumatic fever following a cold, the rheumatism jumped from joint to joint, and he complained of pains about the heart. The area of the transmission of the mitral systolic murmur had extended into the axilla. The heart was enlarged, being 10 cm. in transverse diameter. The

systolic blood-pressure was 92, the diastolic 80. The exercise tolerance was lessened. His tonsils did not seem infected, but were removed as a possible source of infection. Six months later he returned with an acute exacerbation. His weight had dropped from 42 to 38 pounds. There was an influenzal bronchopneumonia present and a double otitis media. These conditions soon cleared up under appropriate treatment in the ward. This patient was confined to bed for several months without any appreciable change in his cardiac condition. Another search was made for foci of infection, and with the aid of the x-ray and dentist a badly abscessed tooth was extracted. In a very short time marked improvement in his general condition was noticed. At the end of six months he was able to walk around with comfort and later even to climb stairs. During the past year he has attended school regularly. Apparently all infection of his heart muscle has subsided. He is gaining in strength and growing normally.

We see in this case the three usual rheumatic manifestations, tonsillitis, chorea, and rheumatic fever. It is of interest to note, however, that the best results were secured after the abscessed tooth had been removed. At eight years of age his weight is 56 pounds, his general nutrition is excellent, his heart muscle well able to take care of the ordinary activity. The prognosis is good. It is of interest to note that four years have been necessary to secure good results. This boy will be observed about every six months. Definite and explicit instructions have been given the mother to keep the boy in bed during mild "colds" or any infectious disease. Splendid co-operation during the last two years has been of great value in securing results.

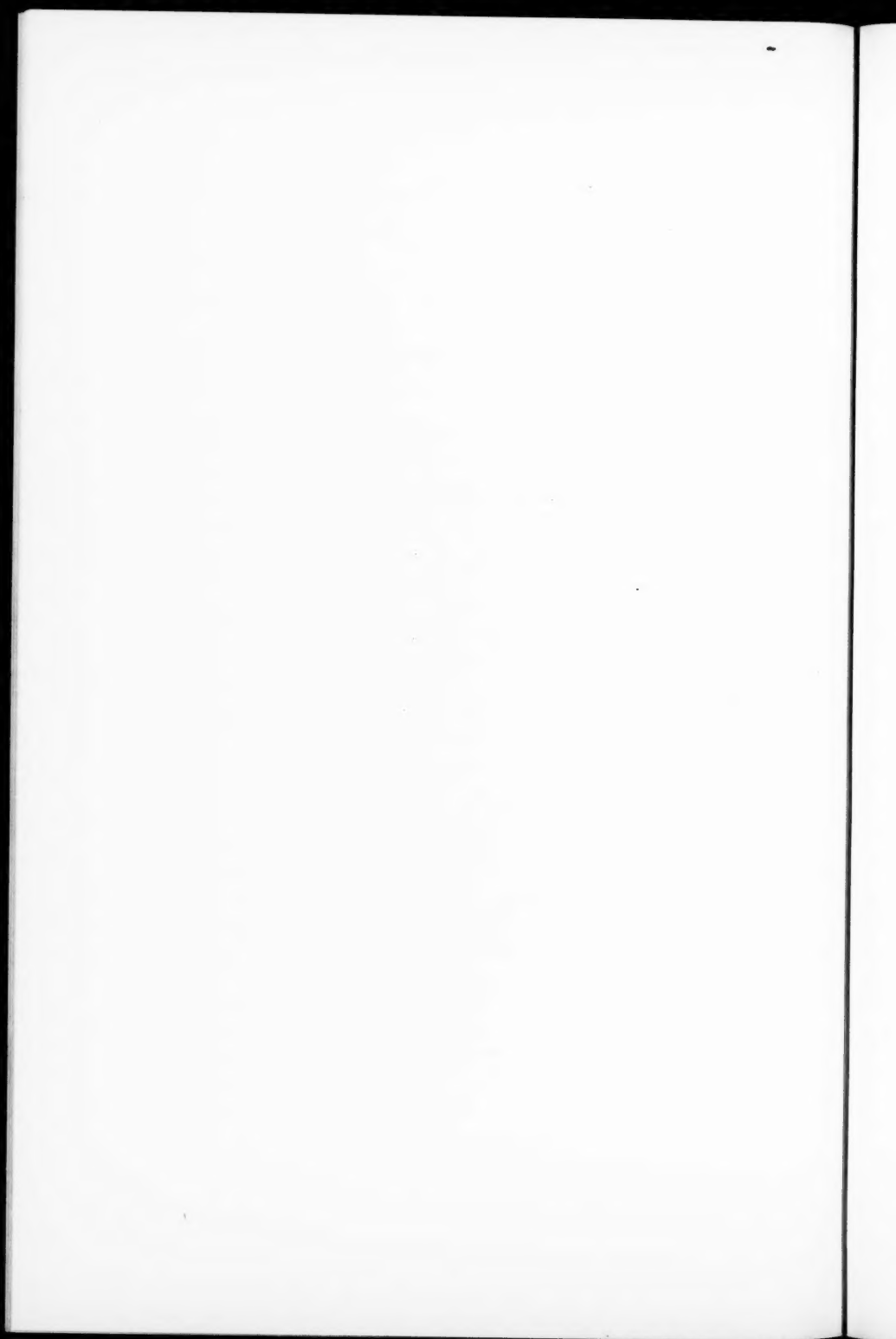
**Case III.**—V. P., a little Italian girl, was first brought to the clinic in January, 1921. The family history was negative. The past personal history showed measles at four years and tonsillectomy at five years of age. At the time of her tonsillectomy there was a severe hemorrhage. In the year following this operation she had had numerous nasal hemorrhages. This was the reason for her admittance to the clinic. Careful nasal examinations

failed to show any bleeding point or ulceration. These hemorrhages usually were small and easily controlled. It was the frequency that caused alarm. There was no history of any rheumatic manifestation, though the child did have a mitral systolic murmur with considerable enlargement of the heart. The child was six years old and weighed 43 pounds. Her heart measured 12 cm. in transverse diameter. The apex-beat was wide-spread and very forceful in character. The child had great difficulty in climbing steps, and limited ability to walk on the level. The mother was carefully instructed as to her care, rest, diet, and exercise. During the first year under observation her weight remained stationary, her pulse-rate and exercise tolerance did not improve, and the heart remained the same size. In March, 1922 she had an influenzal bronchopneumonia, but made a good recovery in several weeks. At the end of this time she was sent to the cardiac house in the country where she remained at rest and graduated exercises for six months. After an abscessed tooth was removed she made good progress and was returned home having gained  $7\frac{1}{2}$  pounds in weight and some cardiac reserve. Several nosebleeds in the next year retarded her progress somewhat, though the tendency of her weight has been upward at the rate of 4 pounds per year. With the increased growth it is interesting to note that her heart actually decreased in size. During the past year she has attended a special school regularly. Transportation has been furnished. Her activity has been hard to restrain and her general appearance has strikingly improved.

Apparently it was the excellent care given at the cardiac home that started this child to improve. The treatment of rest allowed of better nutrition to the body in general and the heart in particular. The child's mother had not fully understood the situation and did not have full control of the child. The doctrine of rest, either complete or limited, the physician finds necessary to inculcate often. In the treatment of cardiac cases absolute control is essential, proper atmosphere, wholesome food, and good hygiene are important.

These cases may be helpful to us all to remember that rheu-

matic manifestations do occur before three years of age and that acquired organic heart disease does occur before five years of age. They also teach that elimination of foci of infection, however small, is most important. The teeth must be carefully examined. In the cardiac cases of second degree, where limitation of activity is necessary, full control in a properly supervised cardiac home in the country is of great value. It is the long rest period that enables the heart to build up its reserve of power. No other measure will serve. All other measures are mere evasions which dodge the real issue. The heart reserve is the crux of heart efficiency in health and disease; the cardiac reserve is the aim of all cardiac therapy.



## CLINIC OF DR. ROBERT P. REGESTER

PENNSYLVANIA HOSPITAL

### STUPOR

GENTLEMEN: I wish to show you 3, and possibly 4, cases which possess one very noticeable symptom in common, namely, stupor; but I think we can show you why we believe them to represent three different diseases.

Stupor in its typical form is characterized by an abeyance of the mental faculties. Stupor does not make its appearance suddenly, but is usually insidious in its onset and is frequently preceded by more or less marked confusion.

DR. REGESTER: Mr. S., will you name the most important and frequent causes of stupor?

MR. S.: Poisoning from narcotic drug or alcohol. Uremia. Concussion of the brain. Diabetes.

DR. R.: Yes. Mr. A., can you add any others?

MR. A.: Epidemic encephalitis. Meningitis. Typhoid fever. Septicemia.

DR. R.: Yes, I believe they all may be included, and perhaps some others, but these, I believe, will be enough for our discussion this morning. The first patient, who is just coming into our clinic, shows this well-marked drowsiness, but, as you will recall, as is necessary in order that the mental state may be considered stupor, he can be aroused, and when aroused he answers questions intelligently.

**Case I.**—White male, married, age forty-eight years. A native of Italy. History obtained from his daughter.

*Family History.*—All of his family in Italy. Daughter does not know anything about them.

*Past History.*—Pneumonia at age of twenty-two years. No history of any other disease.

*Present Illness.*—Onset rather indefinite. Since January 1, 1924 has had morning vomiting. No pain in the abdomen. No bloody vomitus. Appetite since onset has been poor. March 6, 1924 began to complain of pain in epigastric region. Has had frequent vomiting since this date until admission. No nose-bleed. Fever about 100° to 101° F. Always restless. Headache since March 6th. March 15th began to become drowsy, and mumbled while asleep, but if awakened he answered questions clearly. Admitted to the hospital on March 25, 1924.

*Physical Examination.*—Pulse, 86; temperature, 101 $\frac{3}{8}$ ° F.; respirations, 28. Blood-pressure, 104/68. Adult white male. Lying in bed, stuporous, but can be roused to intelligent replies. No dyspnea, cyanosis, or jaundice.

Head, ears, and nose negative.

Eyes: Ocular movements full and equal. No ptosis. Conjunctivæ red and watery. Pupils equal. React well to light and accommodation.

Mouth: Teeth dirty; some loose. Pus exudes from gums around the teeth on pressure. Tongue coated with thick, white coating. Pharynx injected. Tonsils small and atrophied.

Face negative; no paralysis.

Chest: Thick walled. No rose-spots. Expansion fair and equal. Percussion hyperresonant throughout. Breath sounds distant throughout. A few râles at the left base on inspiration.

Heart: No bulging, shock, or thrill. No visible or palpable apex-beat. O. C. D. in 2.1 S.; 2.5 cm. to right of M. S. L.; 3.5 cm. to left of M. S. L. R. B. at the right sternal margin in 41 S. L. B. 11 cm. to left of M. S. L. in 5.1 S. Sounds regular, clear, distant; no murmurs. Blood-pressure 104/678.

Abdomen tympanitic. No rose-spots. Liver dulness extends from 21 to 28 cm. below the clavicle in R. M. L. line. Neither liver nor spleen palpable. No masses. Active abdominal reflexes. Genitalia negative.

Extremities: Pulse 20 to  $\frac{1}{4}$ , regular, good volume. All reflexes active. No ankle-clonus. Babinski negative; no König's



or Prudinski's sign. There is, however, cogwheel resistance in all four extremities.

The laboratory reports at this time were:

Urine: Amber, acid, 1030-1032. Trace of albumin. No sugar, acetone, or diacetic acid. Microscopic examination negative.

Blood-count: Hb., 80 per cent.; R. B. C., 4,600,000; W. B. C., 11,700; polys., 66 per cent.; lymphocytes, 31 per cent.; eosin., 2 per cent.; transitional, 1 per cent. Blood Wassermann negative. Blood-cultures negative after three days.

DR. REGESTER: Now, Mr. S., you suggested some of the diseases which might be responsible. Can we place him in any class?

MR. S.: No. I don't think so.

DR. R.: Is there anything further we might do to clear up the diagnosis?

MR. S.: Yes. Blood chemistry.

DR. R.: Yes, that is correct. Has any one anything else to suggest?

STUDENT: Lumbar puncture.

ANOTHER STUDENT: Eye-ground examination.

DR. R.: Yes, I agree, and all of these examinations have been made.

The blood chemistry: Sugar, 104; urea N., 12.7; creatin, 1.5.

Spinal fluid: Cells, 57. Globulin increased. Sugar increased. Wassermann negative.

Eye examination by Dr. Shoemaker: Pupils equal, ocular movements full. No paralysis. Ophthalmoscopic both eyes. Disks flat, nasal edges not sharply defined. Temporal edges sharply defined. Vessels are good. No hemorrhages, exudates; no hemianopsis.  $\alpha$ -Ray of skull negative for fracture or injury.

DR. R.: Mr. S., will you give us an opinion about this man?

MR. S.: I believe we can rule out diabetes, uremia, concussion of the brain, meningitis, septicemia, typhoid fever.

DR. R.: You would then make a diagnosis of epidemic en-

cephalitis. That is what we have done. There is, however, one important symptom which we have been unable to elicit in this case, and that is diplopia.

In 1922 and 1924 Foster and Cockrell published articles in which they studied the spinal fluids by quantitative methods for sugar, finding that increase in sugar was consistent in encephalitis. This, to my mind, is a great help. It serves to distinguish the condition from tuberculous meningitis in which, according to these authors, just the reverse occurs. Epidemic encephalitis is, of course, an acute infection, mildly contagious, of obscure pathology, showing unusual cerebral symptoms and increasing languor.

This second patient possesses the symptom about which we are concerned this morning, namely, stupor.

**Case II.**—R. A. White male, age forty-three years. Native of Germany. History obtained from his brother. Patient has enjoyed good health until this present illness. Has not been working regularly since March 15, 1924. Has had cold, sore throat, and severe headaches. April 8th he told his brother that he had to get some glasses on account of rapidly failing vision. A physician was called to see patient, and on April 15th found him in a stuporous condition. He was sent to the hospital on this same date.

*Physical Examination.*—Pulse, 80; temperature, 98 $\frac{1}{2}$ ° F.; respirations, (?); blood-pressure, 250/150. Adult white male, lying quietly in bed in deep stupor, from which he can be roused to reply to questions. He speaks slowly, with mumbling, thick speech. No slurring of ends. Breathing is of the Biot type, with apnea of twenty seconds. No jaundice. Skin is dry, thick, and scaly.

Head: Vessels tortuous and distended.

Eyes show arcus senilis; narrowing of left palpebral fissure; pupils react slowly and slightly to light.

Nose negative.

Mouth: Lips dry. Teeth dirty; gums are poor. Pharynx clear. Tonsils well atrophied. Breath is foul and urinous.

Neck: Veins are distended and pulsate. Palpable anterior and posterior glands.

Chest: Very thin walled; expansion fair, equal. Percussion hyperresonant. Breath sounds vesicular. No râles heard.

Heart: No bulging, shock, or thrill. Apex visible in 5.1 S. Palpable 12 cm. to left of midsternal line. Outline cardiac dullness; 2.1 S.; 2 cm. to right of M. S. L.; 4 cm. to left of M. S. L. Right border 4 I. S.  $3\frac{1}{2}$  to right of M. S. L. Left border 13 cm. to left of M. S. L. 5.1 S. Sounds regular; systolic murmur at apex, not transmitted. Systolic aortic murmur heard along right border of sternum. First sound at apex loud and booming. A-2 is accentuated. Blood-pressure 250/150.

Abdomen negative.

Extremities negative.

Urine: Specific gravity 1012-1012. Albumin, heavy cloud. Sugar negative. Microscopic negative except for occ. W. B. C. Blood: Hb., 75; R. B. C., 4,350,000; W. B. C., 12,800.

Wassermann: Blood negative. Spinal fluid negative. Spinal fluid cells 57. Globulin not increased. Sugar, faint reduction.

Blood chemistry: Blood-sugar, 124; urea N., 41.8; creatin, 4.8.

DR. REGISTER: Mr. S., will you give us your opinion concerning this man?

MR. S.: There seems to be no doubt that this is a cardiovascular condition, with uremia.

DR. R.: Yes. I do not believe we have any other alternative but to make this diagnosis.

**Case III.**—The third patient I would like to show you is extremely interesting. His initials are H. F., white male, aged twenty-six, married. Native born. History taken from wife.

*Complaint.*—Pain in abdomen.

*Family history* negative as regards present illness.

*Past History.*—Repeated attacks of tonsillitis until removal of tonsils in January of this year.

*Present Illness.*—Onset rather indefinite. February 6, 1924 began to have dizzy headache, weakness, was drowsy all the time. February 11th to 18th symptoms worse. Sleepy all the time.

No appetite. Bowels constipated. Headache severe. February 21st had nosebleed. During the last four or five days has been sleeping all the time. When aroused answers questions clearly. No dyspnea or jaundice. Slight cyanosis.

Head negative.

Eyes: Pupils dilated. Right is larger than left. React well to light.

Ears and nose negative.

Mouth: Teeth fair, tongue thick, dry, white coating. Pharynx injected.

Neck: Palpable lymph-glands at the angle of the jaw on both sides. Postcervical are not palpable.

Chest: Good expansion. Percussion note resonant throughout. Breath sounds vesicular throughout. No râles. Numerous rose-spots seen.

Heart: No precordial bulging, shock, or thrill. Area of cardiac dullness not increased. Sounds are distant and weak. No murmurs.

Abdomen: Numerous red spots that fade on pressure and then return. Liver edge palpable 2 cm. below the costal margin in right midclavicular line. Spleen dullness increased. Spleen is palpable. Reflexes active. Scar in right inguinal region.

Extremities negative.

Laboratory reports: Urine amber, acid, 1028, light cloud of albumin, sugar negative, microscopic negative.

Blood-count: Hb., 89 per cent; R. B. C., 5,140,000; W. B. C., 3700.

Blood-culture negative.

2/21: Widal for B. typh. Para A and B negative.

2/27: Widal for B. typh. Para A and B negative.

3/4: Widal for B. typh. Para A and B negative.

Wassermann reaction: C plus 4; A plus 4.

DR. REGESTER: MR. A., do you feel that we have a right to express an opinion about this man?

MR. A.: Yes. I should feel that with the temperature, rose-spots, palpable spleen, and a leukopenia that a clinical diagnosis of typhoid fever might be made.

DR. R.: We have made the same deductions, but, at the same time, we must admit that the diagnosis is on an unsound basis until we can prove the presence of typhoid bacillus. It seems to me that we are particularly fortunate in our material today to be able to present these cases in about the same mental state, the cause of which I believe we have demonstrated to be due to three different diseases. At another time we hope to be able to report further on these 3 cases, and either confirm the findings of this morning or give our reasons for the change in the diagnosis.

*April 28th:* Gentlemen, I should like to recall to your attention 3 cases that you saw several weeks ago. All were in a state of stupor when you saw them. In the first man, whom we considered an epidemic encephalitic, we were able to find nothing which was against that diagnosis. He recovered and has been discharged as cured. The second man, with the uremia, grew progressively worse. Urinous odor became more pronounced on the breath. Urine output for twenty-four hours was only 16 ounces. Blood chemistry rose. It had been: Blood-sugar, 124; urea N., 41.8; creatin, 4.8. The last examination was: Blood-sugar 160; urea N., 72.2; creatin, 6.7. He died in uremic coma. The third case I am going to show you again because he presents two rather unusual things. For the past few days he has had a marked hoarseness, almost aphonia, which came on suddenly. The report from the nose and throat department: Nasopharyngitis and a greatly congested larynx. No evidence of paralysis of vocal cords. This raises the question as to whether the laryngeal condition is due to same organism that is responsible for the systemic infection. I think when you saw him before the Widal reaction was negative. Since that time the reaction has become positive and *Bacillus typhosus* has been recovered from the urine and stools. The probable explanation of the aphonia, it would seem, is not that typhoid bacillus has invaded the larynx, but that the edema of the larynx is secondary to the acute esophagitis which is quite frequently found in typhoid fever. This patient presents one other interesting condition.

On March 22d, at 4.45 A. M., he had a sudden drop in temperature, complained of upper abdominal pain, with slight tenderness in upper right quadrant, general resistance, but no rigidity. Blood-count at this time was Hb. 60 per cent., R. B. C. 3,150,000, and W. B. C. 9000. The white count was repeated several times during the day, but no count was obtained above 9400. The chest at this time was clear, but we felt that on account of absence of rigidity and the absence of leukocytosis we were justified in waiting for twenty-four hours in order to clear up the question of perforation. On the next day we were able to hear a friction-rub very low down in the right axilla, and abdominal symptoms were less marked. Fluid rapidly developed, and on March 26th the chest was aspirated of 1000 c.c. of yellow, cloudy fluid, the culture from which showed the presence of *Streptococcus hemolyticus*.

The question some have raised is whether the empyema is an infected transudate. We do not believe so, first, because we were unable to find any evidence of effusion before the beginning of the acute attack, and because of the sharp, sudden onset of the present trouble. He will be kept on the medical side until such time as the material becomes purulent and thick. Aspiration will be done when necessary, and when the discharge thickens he will be transferred to the surgical side for operation.

## CONTRIBUTION BY DR. GEORGE P. MEYER

FROM THE CLINIC OF APPLIED IMMUNOLOGY OF THE OUT-PATIENT  
MEDICAL DEPARTMENT, JEFFERSON HOSPITAL

### ASTHMA

MANY advances in the diagnosis and treatment of asthma and allied conditions have occurred in the last decade, following the application of immunologic knowledge to these so-called atopic disorders. In the Jefferson Hospital Out-Patient Department and Wards we fortunately have been able to observe many hundreds of cases of clinical hypersensitiveness and to help not a few. Our management of these cases, especially the asthmatics, is as follows:

A very painstakingly thorough history is taken in order to determine the primary and secondary etiologic factors.

The primary factors are the atopens or specific substances to which a person is hypersensitive, exposure to which induces symptoms. In our experience ingested materials play a minor rôle, especially in adults, the chief part being assumed by the inhaled atopens, such as pollens, dusts, orris root, animal epithelia, cereals, and others.

The secondary factors include foci of infection, disease in the nose and throat and paranasal sinuses, and pathologic conditions more or less remote which aggravate the symptoms of asthma.

Thorough general physical and special nose and throat examinations are routinely employed, and when indicated the special laboratory facilities readily available are freely used to assist in the study and treatment of the patient as a whole.

Specific tests are then made by the intradermal injection with a fine tuberculin syringe of 1/100 to 1/50 cm. of an extract of

the suspected material or atopen. These extract solutions are made up by the method of Coca,<sup>1</sup> which is roughly as follows:

The suspected material is soaked for twenty-four to forty-eight hours in a solution containing 0.5 per cent. sodium chlorid, 0.4 per cent. phenol, and 0.25 per cent. sodium bicarbonate in distilled water. The solution is then expressed, filtered through paper, and finally undergoes Berkefeld filtration to sterilize, as heat or chemical sterilization may so alter the material as to make it unfit for testing. A positive test is indicated by the formation of an urticarial wheal, with a surrounding zone of erythema. All positive tests must be confirmed at a subsequent visit.

The treatment consists of the removal of the primary and secondary etiologic factors. The primary factors, chiefly the inhalent atopens, are completely removed is possible from the environment of the patient. In those cases in which complete freedom from contact is not attainable, one attempts to hypo-sensitize with repeated injections in ascending doses of extracts of the offending material. If successful, this process makes the patient relatively less susceptible to the atopen. The secondary etiologic factors are treated as indicated. Deflection of a septum is corrected, infected tonsils are removed, abscessed teeth extracted, and general medical and surgical measures applied to the care of the patient as a whole.

Needless to say many interesting problems have presented themselves, and it is our purpose to report several of them and in their discussion offer a few suggestions that may be helpful in the diagnosis and treatment of this troublesome condition.

**Case I.**—A. D. R., white male, aged thirty-nine, a chicken farmer, referred to the clinic October 26, 1922, complaining of asthma.

*Family History.*—Was negative for tendency to atopic hypersensitiveness or other diseases.

*Past History.*—Measles as a boy, since when acuity of hearing has been decreased. Pneumonia at fifteen.

*Present Illness.*—Two years before reporting to the clinic



he had gone on the farm to raise chickens. Shortly after taking up that work he noted that attacks of shortness of breath accompanied his working about in the dust of straw, alfalfa, or chicken feed. In particular did he notice the evil effect of the dust about a threshing machine. At that time handling chickens or cleaning out the chicken houses seemed to cause no trouble. Asthma was more marked in winter. There was complete cessation of symptoms when he was off the farm.

*Physical examination* reveals a well-nourished adult, white male, healthy and active in appearance. General examination was negative except for a few fine râles diffusely scattered throughout his lungs.

*On the first visit* negative intradermal tests were obtained with feathers, cereals, hay, straw, and cow epithelium. At the request of his physician he had brought with him samples of feeds and powders from the farm, and from these extract solutions were prepared. On the second visit, November 23, 1922, he was tested with them, and markedly positive reactions were obtained with two, viz., a poultry powder and a scratch feed. Extracts of house dust, orris and animal danders yielded negative reactions. The most marked reaction of all, however, was elicited with an extract of flaxseed. He was informed of the noxiousness of the substances with which marked reactions were obtained and told to get rid of and avoid future contact with them.

On the third visit, March 1, 1923, he reported that among other offending feeds he had gotten rid of one poultry tonic containing 70 per cent. flaxseed. Relief was prompt and continued for a long while, except for one mild attack attending the handling of clover for chicken feed.

When last seen, July 29, 1924, he reported continued general good health interrupted by only infrequent and mild attacks in cleaning out the chicken house. This difficulty is hard to explain. It has been but lately acquired, as a year or more previous no dyspnea had been caused by that work.

At night there is no interference with sleep, and at no time in the interval has he been incapacitated. He continues to

avoid flaxseed feeds, using instead corn, oats, wheat, and other cereals.

*Comment.*—This case illustrates a type of occupational asthma. It is not infrequent, being most often met in farmers and bakers in whom cereal dusts are the cause.

It has long been a practice in rural districts for persons so affected to wear masks with fine paper filters to free the inspired air of offensive dusts. An unfortunate situation arises when a person trained to one work becomes sensitive to the dusts commonly met in that work. For economic reasons it is often out of the question to change his occupation, and one must make efforts at hyposensitization or the lessening of pathologic susceptibility by repeated injections in ascending dosage of extracts of the causal atopen.

Relief is usually but partial and the patient frequently is forced to make the sorry choice of keeping his job with mild, continued asthma, or seeking work less desirable and remunerative, but likewise less apt to cause asthma.

Our patient, by the elimination of certain offensive materials, was fortunate in securing relief sufficient to make a change of occupation unnecessary.

**Case II.**—M. W., white adult male aged forty-two, a pattern maker, referred by his company physician September 11, 1921.

*Chief complaint* was attacks of shortness of breath and cough, chiefly nocturnal.

*Family history* was negative for any tendency to atopic hypersensitiveness.

*Past history* marked by frequent colds and an attack of influenza in 1918.

*Present Illness.*—Started in May, 1921 with symptoms simulating hay-fever. Periods of trouble with intervals entirely free of symptoms continued until early July, 1921, when there was an abatement in the condition. In late July, however, an attack of asthma occurred which seemed to displace the hay-fever symptoms that have since never reappeared.

During the summer three attacks of asthma occurred last-

ing seven to ten days. One was severe enough to keep the patient from work. These attacks were characterized by cough and shortness of breath and dyspnea and were especially marked nocturnally.

There were no pets or other animals in the house. Feathers, however, were present as a possible cause of trouble. The history was suggestive of hypersensitiveness to the grass pollens. Feathers and house dust likewise fell under suspicion.

*Physical examination* revealed a heavy set somewhat pallid dyspneic adult white male.

Head, including a special nose and throat examination, negative.

Chest and lungs: No marked limitation in expansion, resonant throughout, vocal resonance and fremitus normal, diffuse râles of all types were heard, as is characteristic of asthma.

Heart and circulatory system normal. Blood-pressure 130/100.

Abdomen and extremities negative. Reflexes normal.

*Laboratory Findings.*—Urine negative.

Blood-count: Hemoglobin, 95 per cent.; red blood-cells, 4,800,000; white blood-cells, 7800. Differential count: Polymorphonuclear 61 per cent., small lymphocytes 34 per cent., large lymphocytes 5 per cent.

*Intradermal tests* were done with all the routine inhalant atopens, including pollens, house dust, orris, animal danders, feathers, cereal inhalants, and other special substances, such as tobacco, pyrethrum, flaxseed, peptone, and others. Marked reactions were elicited to none of our inhalant atopens. An extract made of the dust from the home of the patient likewise did not yield a marked reaction.

Feeling that we had missed the real cause of the trouble, we persisted in quizzing the patient with the view of discovering some new substance as a causal factor in his asthma, meanwhile employing such general medical measures as we felt would help. Our efforts were fruitless until one day the patient volunteered the information that whenever he opened a certain drawer of papers at his place of work he sneezed. Upon inquiring further,

we found that the drawer contained pepper which had been put there to protect the papers against mice. An extract solution was made according to the method of Coca from cayenne pepper. Two test injections were made, using 1/100 to 1/50 c.cm. of the undiluted extract solution intradermally. Very marked reactions followed. We felt that we had discovered the cause of the trouble and told him to avoid all contact with pepper. He told us that he never used pepper as a seasoning, although he had not suspected any peculiar idiosyncrasy to it.

On the way home the patient was seized with a constitutional reaction marked by generalized urticaria, angioneurotic edema, coryza, and severe asthma. He had to be assisted home, where he was confined to bed for three days. Following this constitutional reaction in November, 1921 he has been entirely free of trouble except for three mild attacks induced by exposure to pepper. The last of these, in January, 1924, followed the thumbing over of some old cards that had been in contact with pepper.

*Comment.*—Several points in this case deserve comment and discussion. The need for persistence in looking for a cause is emphasized. Over two months diligent quizzing of the patient, giving him our viewpoint of the noxiousness of some unknown agent which it was his job to discover, were necessary for a successful outcome to our search.

Despite the history suggestive of sensitivity to pollens, tests with these substances were uniformly negative.

The dangers of testing and treating with atopen solutions call for consideration. A constitutional reaction to an intradermal test, as reported above, is rather uncommon. Less rare, in fact, too common, are reactions to the therapeutic subcutaneous injections employed to hyposensitize. In an active clinic or practice in this particular field a year seldom goes by without several alarming reactions. Death is known to have followed such a reaction. Several precautions suffice to lessen the frequency and danger of this *bête noir* of the immunologist. Briefly summarized, they are as follows:

In testing new substances under investigation use dilute solutions.

Be particularly careful in the use of atopens, whose use has most often been marked by constitutional reactions, such as pollens, animal danders, and orris.

Avoid too many tests at one sitting.

Avoid intravenous and intramuscular injections.

Always have adrenalin and stimulants readily available for use in the cases that unfortunately and unavoidably do occur.

**Case III.**—E. B., white boy of sixteen, presented himself at the clinic September 24, 1921, complaining of asthma.

*Family history* was positive for the atopic tendency in that the patient's paternal grandmother had asthma.

*Past history* negative except for an attack of measles as a child.

*Present Illness.*—Asthma started when the patient was four years old. Attacks marked by dyspnea and cough occurred about once or twice a week and lasted twenty-four to seventy-two hours. In the intervals between attacks there was entire freedom from symptoms. Attacks recurred throughout the year, but there was an exacerbation of symptoms in the late summer and fall, attended by some sneezing and watering of the eyes. Changes in residence had been tried by the patient as a method of relief with but little influence on the course of the disease.

In the country, at a seashore resort, or at home in the city the trouble varied but little. From childhood the condition had persisted, with almost no change in the frequency or severity of attacks until a particularly bad time of it during the late summer and early fall of 1921 forced the patient to give up a good job and induced him, then sixteen years old, to report for treatment. At home there were as possible causes of asthma feathers and a cat and house dust.

*Comment on the History.*—The presence of asthma in the paternal grandmother illustrates the influence of heredity in this disease. In the majority of patients, if one is sufficiently diligent in inquiring, one can discover a transmitted tendency

to one of the atopic disorders, such as asthma, urticaria, or hay-fever. The earlier in life the disease appears, in our patient before five years of age, the more potent the hereditary influences. This was first pointed out by Cooke<sup>1</sup> who proved that this type of hypersensitiveness seems to be transmitted as a dominant gen according to the Mendelian laws of heredity. This attribute of atopy has been amply proved by other observers and ourselves.

The exacerbation of symptoms in the late summer and fall would lead us to suspect the presence of hypersensitiveness to the pollen of some plant blooming at this time, chiefly in this section of the country, ragweed.

Because of the fact that changes in residence produced no alleviation in symptoms, we would presume that the cause of the perennial trouble was not solely in the home environment of the patient.

The presence of the cat in the home of the patient would lead us to suspect it as a possible cause of asthma and to be particularly cautious in testing to use diluted cat epithelium extract solution to avoid the possibility of constitutional reactions.

*Physical examination* reveals a rather thin, tall, somewhat dyspneic white boy.

Head, including a special nose and throat examination, negative.

Chest, lungs: Some general limitation of expansion, no percussion changes, rhoncal fremitus generally felt, many râles heard throughout as is typical of asthma.

Heart and circulatory system negative for disease.

Blood-pressure, 100/60.

Abdomen and extremities negative. Reflexes normal.

*Laboratory Findings.*—Urine negative.

Blood Wassermann negative.

Blood-count: Hemoglobin, 90 per cent.; red blood-cells, 4,900,000; white blood-cells, 9000. Differential: Polymorphonuclear leukocytes 62 per cent., small lymphocytes 32 per cent., large lymphocytes 4 per cent., eosinophils 2 per cent.

x-Ray of the chest reveals some old tuberculous deposits in

the apices, general peribronchial thickening, with some emphysema in the lower lobes.

*Skin tests* were made, with the following results:

*Marked reactions* were obtained with ragweed, confirming our suspicions regarding the cause of the exacerbation of symptoms in the late summer and fall.

Cat epithelium and duck feathers; to both of which factors the patient was exposed.

Stock dust solution, which in our experience elicits more often than any other atopen a marked skin reaction.

An extract from the patient's home dust yielded the most marked reaction of all.

*Moderate reactions* were present to chicken feathers, horse epithelium, and pyrethrum (a common ingredient in bug powders).

*Slight or negative* reactions to the other inhalant atopens tested, viz., other pollens, animal danders, orris, cereals, and others.

Only those substances yielding marked skin reactions characterized by the appearance of an urticarial wheal with pseudopodia and a surrounding zone of hyperemia were considered of primary etiologic importance.

*Management of Case.*—The patient presented himself at a time when ragweed pollen might still operate to cause trouble. A few doses of that extract in ascending strength at intervals of three days sufficed to bring about a decided alleviation of symptoms. However, attacks did recur, though modified in frequency and severity, and this perennial trouble next engaged our attention. Following the therapeutic principle of removing the cause, the cat and the feathers were eliminated from the home of the patient and required no further consideration. He was urged to make his home surroundings as dust free as possible by getting rid of dust-catching articles of furniture and floor covering, and by frequent dustings and cleansings, especially of his bedroom.

However, there always remains a residuum of dust in the air that is not removable and which demands efforts at hyposensitization. Hyposensitization or the decreasing of pathologic hy-

persensitiveness, to an atopen, as mentioned before, is brought about by repeated injections in ascending dosage of a solution of the offending material. In this patient (at first, to hyposensitize), we used a stock dust extract, one that is made of a mixture of dusts which had elicited marked skin reactions in other asthmatics. Later we used an "autogenous extract"; this we made by the method of Coca, of dust collected by broom or sweeper from the home of the patient. When 1/100 to 1/50 cm. of this autogenous dust extract solution was injected intradermally it uniformly yielded the most marked reaction elicited in this patient.

Therefore we felt that it was probably superior to stock dust extract for therapeutic purposes. Following our usual custom, 1/10c.cm. was injected subcutaneously and the injection repeated at weekly intervals, each one increased by 1/10 c.cm. over the preceding. Improvement in the patient was steady and gratifying. After the 1 cm. dose was reached no further increases were made. Improvement being maintained, the intervals between injections were increased to two weeks, then three, then four. Even in those cases entirely free of symptoms we have recommended monthly injections of 1 c.cm. for a year or more.

However, this patient improved so that it was difficult to enforce regular attendance. He has had virtually no treatment after the first few months except the yearly course of ragweed injections, but has remained symptom free and devoid of physical signs of asthma for at least a year.

*Comment.*—This case illustrates an extremely common form of clinical hypersensitiveness, namely, asthma due to house dust. In an analysis of 235 cases of asthma<sup>3</sup> recently reported by the author, house dust was found as a cause in 57 per cent. of the cases, either alone or with other atopens. In our experience it is the most common cause of asthma. The treatment of this type must be long continued, and the steady co-operation on the part of the patient in cleaning up his home and making it dust free is absolutely essential. Over 60 per cent. of the dust cases in the analysis referred to were considerably relieved, but further improvement in our results should follow diligent study



and work in this important field of medicine. It must not be inferred from the happy results obtained in the 3 cases reported that all asthmatics present a problem so easily solved or so readily helped. They are merely presented as cases with certain interesting features whose discussion may prove profitable.

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